

In search for novel agents in therapy of tropical diseases and human immunodeficiency virus

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Supporting material

Content:

Spectroscopic data of all compounds: ^1H and ^{13}C NMR, IR.

Combustion analysis data

Dimethyl (2*R*,6*S*)-4-oxo-2,6-di(pyridin-2-yl)piperidine-3,5-dicarboxylate (1)

C₁₉H₁₉N₃O₅ (369.4 g/mol), yield: 33 % (67 %); ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) 2.94 (t, 1H, ³J = 12.3, NH); 3.53 (s, 6H, COOCH₃); 4.25 (d, 2H, ³J_{aa} = 10.5, CHC=O); 4.62 (dd, 2H, ³J = 12.3, ³J_{aa} = 10.5, CHNH); 7.32 (ddd, 2H, J = 1.0, J = 4.8, J = 7.6, H6' or H4'); 7.45 (d, 2H, J = 7.8, H6' or H4'); 7.78 (dt, 2H, J = 7.6, J = 1.8, H5'); 8.50-8.56 (m, 2H, H3'). ¹³C NMR (DMSO-d₆, δ = ppm) 51.6 (COOCH₃); 61.6 (CHC=O); 63.0 (CHNH); 123.2 (C4'/C6'); 137.0 (C5'); 148.9 (C3'); 158.0 (C1'); 168.6 (COOCH₃); 202.1 (C=O). IR (cm⁻¹) 3296; 3021; 2954; 1739; 1701; 1432; 1335; 1213; 1110; 816; 776. mp. 175 °C.

Dimethyl (2*R*,6*S*)-1-allyl-4-oxo-2,6-di(pyridin-2-yl)piperidine-3,5-dicarboxylate (2)

C₂₂H₂₃N₃O₅ (409.5 g/mol), yield: 87 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.00 (m, 2H, NCH₂); 3.59 (s, 3H, COOCH₃); 3.74 (s, 3H, COOCH₃); 4.18 (d, 1H, J = 10.3, CHC=O); 4.68 (d, 1H, J = 10.3, CHNH); 4.97 (s, 1H, NCHCq); 5.19 (ddd, 2H, J = 17.3, J = 10.1, J = 1.2, =CH₂); 5.79 (m, 1H, J = 17.3, J = 10.1, NCH₂CH=); 7.07- 7.19 (m, 2H, H_{aromat.}); 7.29 (m, 1H, H_{aromat.}); 7.52- 7.71 (m, 3H, H_{aromat.}); 8.43 (m, 1H, H_{aromat.}); 8.60 (m, 1H, H_{aromat.}); 12.52 (s, OH). ¹³C NMR (CDCl₃, δ = ppm) 44.32 (CHC=O); 50.53 (NCH₂); 51.76, 52.5 (COOCH₃); 59.43 (CHNCH₂); 60.38 (H₂CNCH); 97.78; 117.68 (=CH₂); 121.84; 122.20; 122.76; 123.06 (C4'/C6'); 135.86 (NCH₂CH=); 136.02; 136.12 (C5'); 148.13; 148.83 (C3'); 158.24 (C1'); 161.32 (C1'); 167.33 (COOCH₃); 171.12, 172.05 (COOCH₃). IR (cm⁻¹) 3040; 3000; 1720; 1650; 1430; 1360; 1250; 1005; 980; 825; 770. mp. 133 °C.

Dimethyl (2*R*,6*S*)-1-(2-hydroxyethyl)-4-oxo-2,6-di(pyridin-2-yl)piperidine-

3,5-dicarboxylate (3) C₂₁H₂₃N₃O₆ (413.4 g/mol), yield: 55 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 2.58-2.68 (m, 2H, CH₂CH₂OH); 3.35-3.43 (m, 1H, CH₂CH₂OH); 3.63 (s, 3H, CqCOOCH₃); 3.67-3.76 (m, 1H, CH₂CH₂OH); 3.74 (s, 3H, CHCOOCH₃); 4.26 (d, 1H, J = 10.6, CHCHCOOCH₃); 4.46 (s, 1H, CH₂CH₂OH); 4.55 (d, 1H, J = 10.6, CHCHCOOCH₃); 5.03 (s, 1H, CqCH); 7.08-7.14 (m, 2H, H3'' and H5''); 7.19-7.25 (m, 1H, H5'); 7.33 (d, 1H, J = 7.8, H3'); 7.55 (td, 1H, J = 7.7, J = 1.8, H4''); 7.69 (td, 1H, J = 7.7, J = 1.8, H4'); 8.40-8.47 (m, 1H, H6''); 8.65-8.72 (m, 1H, H6'). ¹³C NMR (CDCl₃, δ = ppm) 44.4 (CHCHCOOCH₃); 48.6 (CH₂CH₂OH); 52.0 (CqCOOCH₃); 52.7 (CHCOOCH₃); 59.3 (CHCHCOOCH₃); 60.2 (CH₂CH₂OH); 61.2 (CqCH); 97.1 (Cq=C-

OH); 121.8 (**C3'**); 122.4 (**C5'**); 122.7, 124.1 (**C3''/C5''**); 136.6 (**C4'/C4''**); 148.4 (**C6''**); 149.8 (**C6'**); 157.5, 161.6 (**C2'/C2''**); 169.6 (Cq=COH); 171.3, 172.1 (C=O). **IR** (cm⁻¹) 3333; 2930; 1726; 1437. mp. 135 °C.

Dimethyl (2*R*,6*S*)-1-(2-hydroxypropyl)-4-oxo-2,6-di(pyridin-2-yl)piperidine-3,5-dicarboxylate (4) C₂₂H₂₅N₃O₆ (427.4 g/mol), yield: 39 %; keto-enol ratio: 1:3. **¹H NMR** (CDCl₃, δ = ppm, *J* = Hz) 1.49 (qu, 2H, *J* = 6.8, CH₂**CH**₂CH₂OH, ketone); 1.59 (qu, 2H, *J* = 6.7, CH₂**CH**₂CH₂OH, enol); 2.23-2.35 (m, 2H, **CH**₂CH₂CH₂OH, ketone); 2.23-2.35, 2.42-2.49 (2m, each 1H, **CH**₂CH₂CH₂OH, enol); 3.15-3.30 (m 2H, CH₂CH₂**CH**₂OH, ketone); 3.15-3.30, 3.36-3.42 (2m, each 1H, CH₂CH₂**CH**₂OH, enol); 3.59 (2s, each 3H, COO**CH**₃, enol); 3.64 (s, 6H, COO**CH**₃, ketone); 4.10 (dd, 1H, *J* = 0.8, *J* = 10.6, **CH**COOCH₃, enol); 4.25 (d, *J* = 6.6, **CH**COOCH₃, ketone); 4.27-4.32 (m, 1H, CH₂**OH**, enol); 4.37 (d, 1H, *J* = 10.6, N**CH**CH, enol); 4.73 (d, 2H, *J* = 6.6, N**CH**CH, ketone); 4.93 (s, 1H, N**CH**Cq, enol); 7.22-7.36 (m, 2H, **H3''** and **H5''**, enol, 1H, **H5'**, enol, 2H, **H5**, ketone); 7.49 (d, 2H, *J* = 7.8, **H3**, ketone); 7.67 (d, 2H, *J* = 8.1, **H3'**, enol); 7.73 (td, 1H, *J* = 7.7, *J* = 1.9, **H4''**, enol); 7.82-7.89 (m, 2H, H4, ketone, 1H, **H4'**, enol); 8.39-8.44 (m, 1H, **H6''**, enol); 8.49-8.54 (m, 2H, H6, ketone, 1H, **H6'**, enol); 12.21(s, 1H, C=C-**OH**). **¹³C NMR** (CDCl₃, δ = ppm) 30.6 (CH₂**CH**₂CH₂OH, ketone); 31.4 (CH₂**CH**₂CH₂OH, enol); 42.7 (**CH**C-OH, enol); 43.7 (N**CH**₂CH₂CH₂OH, enol); 44.6 (N**CH**₂CH₂CH₂OH, ketone); 51.6 51.7 (O**CH**₃, enol); 52.0 (O**CH**₃, ketone); 56.5 (**CH**C=O, ketone); 58.3 (CH₂CH₂CH₂OH, ketone); 58.7 (CH₂CH₂**CH**₂OH, enol); 59.3 (N**CH**CH, enol); 60.0 (N**CH**qC, enol); 63.2 (N**CH**CH, ketone); 98.0 (Cq=COH, enol); 122.2, 122.5, 122.7, 123.0 (**C3'/C3''**, **C5'/C5''**, enol); 123.0, 123.4 (**C3**, **C5**, ketone); 136.6, 136.7 (**C4'/C4''**, enol); 137.1 (**C4**, ketone); 148.0; 148.3 (**C6'/C6''**, enol); 148.5 (**C6**, ketone); 157.4 (**C2**, ketone); 161.4, 157.9 (**C2'/C2''**, enol); 166.2 (COO**CH**₃, ketone); 169.0 (Cq=C-OH, enol); 170.6, 171.8 (COO**CH**₃, enol); 198.6 (C=O, ketone); **IR** (cm⁻¹) 3524; 2957; 1736; 1438. mp. 136 °C.

Dimethyl (2*R*,6*S*)-1-[2-(2-hydroxyethoxy)ethyl]-4-oxo-2,6-di(pyridin-2-yl)piperidine-3,5-dicarboxylate (5): C₂₃H₂₇N₃O₇ (457.5 g/mol), yield: 63 %; **¹H NMR** (CDCl₃, δ = ppm, *J* = Hz) 2.44- 2.51 (m, 1H,); 2.67- 2.76 (m, 1H, N**CH**₂**CH**₂); 3.44- 3.58 (m, 3H, N**CH**₂CH₂O**CH**₂); 3.60 (s, 3H, COO**CH**₃); 3.75 (s, 3H, COO**CH**₃); 3.77- 3.80 (m, 2H,); 3.62- 3.69 (m, 1H,); 4.20 (d, 1H, *J* = 10.6, O=C**CH**COH); 4.59 (d, 1H, *J* = 10.6,

CHNCH); 5.41 (s, 1H, *NCHCq*); 7.08 (t, 1H, *H4''*); 7.22- 7.29 (m, 2H, *H6''/H4'*); 7.45 (d, 1H, *H6'*); 7.53 (dt, 1H, *H5''*); 7.72 (t, 1H, *H5'*); 8.42 (d, 1H, *H3''*); 8.68 (d, 1H, *H3'*); 12.57 (s, *OH*). ¹³C NMR (CDCl₃, δ = ppm) 45.29 (O=CCHCOH); 48.63 (*NCH₂CH₂*); 53.37, 53.96 (COOCH₃); 60.97 (*CHNCH*); 62.74 (*NCH₂CH₂OCH₂CH₂OH*); 64.36 (*NCHCq*); 73.18 (*NCH₂CH₂*); 73.98 (*NCH₂CH₂OCH₂CH₂OH*); 98.83 (*CqCOH*); 123.82 (*C6'*); 123.87 (*C4'*); 123.94 (*C6''*); 125.20 (*C4''*); 137.67 (*C5'*); 138.38 (*C5''*); 149.57 (*C3''*); 150.61 (*C3'*); 159.61 (*C1'*); 162.15 (*C1''*); 170.17 (*CqOH*); 173.02, 173.58 (COOCH₃). IR (cm⁻¹) 3020; 3000; 2830; 1610; 1520; 1370; 1117; 821; 740. mp. 175°C.

4-[(2R,6S)-3,5-bis(methoxycarbonyl)-4-oxo-2,6-di(pyridin-2-yl)piperidin-

1-yl]butanoic acid (6): C₂₃H₂₅N₃O₇ (455.5 g/mol), yield: 70%; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.71- 1.83 (m, 1H, *NCH₂CH₂*), 1.89- 2.40 (m, 2H, *NCH₂CH₂CH₂*), 2.28- 2.47 (m, 2H, *NCH₂CH₂CH₂*), 2.51- 2.61 (m, 1H, *NCH₂*), 3.61 (s, 3H, COOCH₃); 3.74 (s, 3H, COOCH₃); 4.23 (d, 1H, J = 10.6, *CHC=O*); 4.52 (d, 1H, J = 10.6, *CHNH*); 5.06 (s, 1H, *NCHCq*); 7.08- 7.18 (m, 2H, *H_{aromat.}*); 7.28- 7.32 (t, 1H, *H_{aromat.}*); 7.50- 7.59 (m, 2H, *H_{aromat.}*); 7.78 (dt, 1H, *H_{aromat.}*); 8.42 (d, 1H, *H_{aromat.}*); 8.71 (d, 1H, *H_{aromat.}*); 12.54 (s, *OH*). ¹³C NMR (CDCl₃, δ = ppm) 23.70 (*NCH₂CH₂*); 32.59 (*NCH₂CH₂CH₂*); 43.96 (*CHCqOH*); 46.76 (*NCH₂*); 52.12, 52.71 (COOCH₃); 59.64 (*CHNCH₂*); 60.50 (*H₂CNCH*); 97.10 (*NCHCq*); 122.73 (*C6''*); 122.97 (*C4'*); 123.31 (*C6'*); 124.02 (*C4''*); 136.59 (*C5''*); 137.74 (*C5'*); 148.33 (*C3''*); 148.75 (*C3'*); 157.79 (*C1''*); 160.26 (*C1'*); 168.98 (*CqOH*); 171.50, 172.04 (COOCH₃); 176.83 (COOH). IR (cm⁻¹) 3030; 2980; 1710; 1620; 1430; 1350; 1210; 950; 845; 700. mp. 169°C.

8-[(2R,6S)-3,5-bis(methoxycarbonyl)-4-oxo-2,6-di(pyridin-2-yl)piperidin-

1-yl]octanoic acid (7): C₂₅H₂₉N₃O₇ (483.5 g/mol), yield: 43 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) keto-enol ratio: 1:5, ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.99- 1.09 (m, 2H, *CH₂*, enol); 1.16- 1.34 (m, 2H, *CH₂*, enol); 1.36- 1.45 (m, 2H, *CH₂*, enol); 2.05- 2.10 (m, 2H, *CH₂*, enol); 2.14- 2.21 (m, 2H, *CH₂*, enol); 2.39- 2.45 (m, 2H, *NCH₂CH₂*, enol); 3.58 (s, 6H, COOCH₃, enol); 3.64 (s, 6H, COOCH₃, ketone); 4.11 (d, 1H, J = 10.5, *CHCqOH*, enol); 4.27 (d, 2H, J = 6.8, *CHC=O*, ketone); 4.36 (d, 1H, *CHNCH*, J = 10.5, ketone, *CHNCH*, enol); 4.71 (d, 2H, J = 6.8, *NCHCH*, ketone); 4.89 (s, 1H, *NCHCq*, enol); 7.20-7.35 (m, 2H, *H6'/H6''*, enol, 2H, *H4'/H4''*, enol, 2H, *H4'*, ketone); 7.48 (d,

2H, **H6'**, ketone); 7.67- 7.75 (m, 2H, **H6'/H6''**, enol, 1H, **H5'/H5''**, enol); 7.82-7.88 (m, 2H, **H5'**, ketone, 2H, **H5'/H5''**, enol); 8.42 (d, 1H, **H3'/H3''**, enol); 8.51 (m, 2H, **H3'/H3''**, ketone and enole). ¹³C NMR (CDCl₃, δ = ppm) 24.0 (**CH**₂, enol); 25.6 (**CH**₂, ketone); 25.7 (**CH**₂, enol); 26.3 (**CH**₂, ketone); 26.8 (**CH**₂, ketone); 30.5 (**CH**₂, ketone); 30.7 (**CH**₂, enol); 33.6 (**CH**₂, enol); 46.0 (**CH**₂, **C5'**, enol); 51.8 (**CH**₂, **C5'**, ketone); 51.9 (**COOCH**₃, enol); 52.2 (**COOCH**₃, ketone); 56.6 (**CHC=O**, ketone); 59.5 (**NCHCH**, enol); 60.3 (**NCHCq**, enol); 63.3 (**NCHCH**, ketone); 98.0 (**Cq=C-OH**, enol), 122.2, 122.6, 122.7, 123.1 (**C3'/C3''** and **C5'/C5''**, enol); 123.0, 123.4 (**C3** and **C5**, ketone); 136.6, 136.7 (**C4'/C4''**, enol); 137.1 (**C4**, ketone); 148.0, 148.2 (**C6'/C6''**, enol); 148.5 (**C6**, ketone); 157.4 (**C2**, ketone); 157.9, 161.6 (**C2'/C2''**, enol); 166.0 (**Cq=C-OH**, enol); 169.0 (**COOCH**₃, ketone); 170.6, 171.8 (**COOCH**₃, enol); 174.4 (**COOH**); 198.6 (**C=O**). IR (cm⁻¹) 3013; 2940; 2858; 1737; 1254. mp. 130 °C.

Dimethyl (2R,6S)-4-oxo-2,6-di(pyridine-2-yl)-1-(pyridine-2-yl-methyl)-piperidine-3,5-dicarboxylate (8): C₂₅H₂₄N₄O₅ (460.5 g/mol), yield: 47%; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.51 (d, 1H, **NCH**₂); 3.53 (d, 1H, **NCH**₂); 3.61 (s, 6H, **COOCH**₃); 4.12 (d, 2H, ³J_{aa} = 10.5, **CHCOOCH**₃); 4.71 (d, 2H, ³J_{aa} = 10.9, **CHNCH**); 7.17 (t, 2H, **H5'/5''**); 7.26-7.31 (m, 2H, **H6'/6''**); 7.66-8.10 (m, 2H, **H3'/3''** or **H4'/4''**); 8.64 (t, 2H, **H4'/4''** or **H3'/3''**). ¹³C NMR (CDCl₃, δ = ppm) 53.6 (**COOCH**₃); 55.8 (**CH**₂); 62.9 (**CHC=O**); 67.9 (**NCH**); 123.7, 123.9 (**C2'/2''/C4'/4''**); 130.3 (**C5'/5''**); 136.3 (**C6'/6''**); 145.3 (**C1'/1''**); 148.4 (**C3'/3''**); 170.1 (**COOCH**₃); 192.4 (**C=O**). IR (cm⁻¹) 3020; 2980; 1710; 1640; 1500; 1405; 1310; 1119; 869; 727; 668. mp. 152-153 °C.

Dimethyl (2R,6S)-1-benzyl-4-oxo-2,6-di(pyridin-2-yl)piperidine-3,5-dicarboxylate (9): C₂₆H₂₅N₃O₅ (459.5 g/mol), yield: 65%; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.53 (s, 2H, **NCH**₂); 3.62 (s, 3H, **COOCH**₃); 3.68 (s, 3H, **COOCH**₃); 3.94 (d, 2H, **CHCOOCH**₃); 4.72 (d, 2H, **NCH**); 6.69-6.75 (m, 2H, **CH_{Benzyl}**); 6.95-6.99 (m, 3H, **CH_{Benzyl}**); 7.27 (t, 2H, **H5'/5''**); 7.46-7.51 (m, 2H, **H6'/6''**); 7.96-8.13 (m, 2H, **H3'/3''** or **H4'/4''**); 8.36 (t, 2H, **H4'/4''** or **H3'/3''**). ¹³C NMR (CDCl₃, δ = ppm) 53.2 (**COOCH**₃); 54.8 (**CH**₂); 64.6 (**CHC=O**); 69.7 (**NCH**); 122.7, 123.0 (**C2'/2''/C4'/4''**); 127.4, 128.3, 128.5 (**CH_{Benzyl}**); 134.3 (**C5'/5''**); 135.4 (**C6'/6''**); 138.6 (**Cq_{Benzyl}**); 143.1 (**C1'/1''**); 147.2 (**C3'/3''**); 169.7 (**COOCH**₃); 193.9 (**C=O**). IR (cm⁻¹) 2980; 1728; 1657; 1531; 1342; 1146; 836; 791; 726. mp. 154 °C.

Dimethyl (2*R*,6*S*)-1-allyl-4-hydroxy-2,6-bis(4-nitrophenyl)-1,2,3,6-tetrahydropyridine-3,5-dicarboxylate (10): C₂₄H₂₃N₃O₉ (497.5 g/mol); yield: 39 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 2.70-2.96 (NCH₂CH=CH₂); 3.54, 3.59 (2s, 3H, COOCH₃); 3.90 (dd, 2H, ³J_{aa} = 9.9, ³J = 2.0, CHCOOCH₃); 4.42 (d, 2H, J = 9.6, NCH₂CH=CH₂); 4.86-4.95 (m, 2H, NCHCq, *H_B*); 5.23 (dd, 1H, ³J_{AC} = 10.2, ²J_{AB} = 1.4, *H_A*); 5.71-5.86 (m, 1H, *H_C*); 7.53-7.59 (m, 4H, *H3'/3"*, *H5'/H5"*); 8.15-8.24 (m, 4H, *H6'/6"*, *H2'/H2"*); 12.24 (OH). ¹³C NMR (CDCl₃, δ = ppm) 51.5 (NCH₂CH=CH₂); 51.9, 52.7 (COOCH₃); 55.3 (CHCOH); 59.7 (NCHCq); 62.6 (NCHCH); 101.4 (Cq=COH); 121.1 (NCH₂CH=CH₂); 123.4, 124.2 (C6'/6", C2'/2"); 129.6, 130.1 (C5'/5", C3'/3"); 130.2 (NCH₂CH=CH₂); 145.9, 151.0 (C4'/4"); 147.4, 148.2, (C1'/1"); 165.6 (Cq=COH); 168.6, 170.5 (C=O). IR (cm⁻¹) 2953; 1733; 1665; 1518; 1439; 1346; 1243; 696. mp.154-155 °C.

Diethyl (2*R*,6*S*)-1-allyl-4-hydroxy-2,6-bis(4-nitrophenyl)-1,2,3,6-tetrahydropyridine-3,5-dicarboxylate (11): C₂₆H₂₇N₃O₉, (525.5 g/mol) yield: 28 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.00-1.07 (m, 6H, COOCH₂CH₃); 2.81-2.98 (m, 2H, NCH₂); 3.95-4.07 (m, 5H, COOCH₂CH₃, CHC-OH); 4.44 (d, 2H, ³J_{aa} = 9.9, NCHCH); 4.86-4.95 (m, 2H, NCHCq, *H_B*); 5.25 (dd, 1H, ³J_{AC} = 12.2, ²J_{AB} = 0.9, *H_A*); 5.75-5.88 (m, 1H, *H_C*); 7.57-7.67 (m, 4H, *H3'/3"*, *H5'/5"*); 8.17-8.25 (m, 4H, *H2'/2"*, *H6'/6"*); 12.38 (OH). ¹³C NMR (CDCl₃, δ = ppm) 14.0, 14.1 (COOCH₂CH₃); 51.4 (NCH₂); 55.1 (NCHCH); 61.4, 61.8 (COOCH₂CH₃); 62.2, 63.0 (NCH); 101.0 (C=COH); 123.3, 124.1 (C2'/2", C6'/6"); 123.9 (NCHCH=CH₂); 129.8 (NCHCH=CH₂); 130.0, 130.5 (C3'/3", C5'/5"); 147.5 (C4'/4"); 148.2 (C1'/1"); 165.9 (C=COH); 168.1, 170.1 (C=O). IR (cm⁻¹) 2981; 2863; 1736; 1661; 1518; 1344; 1245; 700. mp.150-151 °C.

Dimethyl (2*R*,6*S*)-1-benzyl-4-hydroxy-2,6-bis(4-nitrophenyl)-1,2,3,6-tetrahydropyridine-3,5-dicarboxylate (12): C₂₈H₂₅N₃O₉ (547.6 g/mol), yield: 12 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.52, 3.66 (2d, each 1H, NCH₂); 3.55, 3.59 (2s, each 3H, COOCH₃); 3.95 (dd, 1H, ³J_{aa} = 9.6, ³J = 1.8, NCHCH); 4.49 (d, 1H, ³J_{aa} = 9.6, NCHCH); 4.79 (d, 1H, ⁴J = 1.5, NCHCq); 6.78-6.83 (m, 2H, CH_{Benzyl}); 7.05-7.15 (m, 3H, CH_{Benzyl}); 7.42-7.52 (m, 4H, *H3'/H3"*, *H5'/H5"*); 8.06-8.11 (m, 4H, *H2'/H2"*, *H6'/H6"*); 12.27 (s, 1H, OH). ¹³C NMR (CDCl₃, δ = ppm) 52.0; 52.7 (COOCH₃); 54.5 (NCHCH); 56.5 (NCH₂); 61.6 (NCHCH); 64.7

(NCHCq); 101.3 (C=COH); 123.2, 123.8 (C2'/C2'', C6'/C6''); 127.5, 128.4, 129.0 (CH_{Benzyl}); 129.7, 130.0 (C3'/C3'', C5'/C5''); 137.0 (Cq_{Benzyl}); 146.4 (C4'/C4''); 151.3 (C1'/C1''); 165.8 (C=COH); 168.5, 170.4 (C=O). IR (cm⁻¹) 2833; 1740; 1657; 1516; 1444; 1344; 1253; 731; 695. mp. 163-171 °C.

Diethyl (2R,6S)-1-benzyl-4-hydroxy-2,6-bis(4-nitrophenyl)-1,2,3,6-

tetrahydropyridine-3,5-dicarboxylate (13): C₃₀H₂₉N₃O₉ (575.7 g/mol), yield: 7 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.10-1.11 (m, 6H, COOCH₂CH₃); 3.49-3.72 (2d, each 1H, ²J = 14.9, NCH₂); 3.95-4.10 (m, 5H, COOCH₂CH₃, NCHCH); 4.48 (d, 1H, ³J_{aa} = 9.6, NCHCH); 4.86 (d, 1H, ⁴J = 1.5, NCHCq); 6.74-6.80 (m, 2H, CH_{Benzyl}); 7.02-7.13 (m, 3H, CH_{Benzyl}); 7.43-7.54 (m, 4H, H3'/3'', H5'/5''); 8.04-8.12 (m, 4H, H2'/2'', H6'/6''); 12.39 (OH). ¹³C NMR (CDCl₃, δ = ppm) 14.0, 14.1 (CH₂CH₃); 54.7 (CHCOH); 56.5 (NCH₂ Benzyl); 61.4, 61.8 (CH₂CH₃); 62.2 (NCHCH); 65.1 (NCHCq); 101.2 (C=COH); 123.2, 123.7 (C2'/2'', C6'/6''); 127.4, 128.3, 128.8 (CH_{Benzyl}); 130.0, 130.3 (C3'/3'', C5'/5''); 137.0 (Cq_{Benzyl}); 146.1, 151.2 (C1'/1''); 147.1, 148.0 (C4'/4''); 166.1 (C=COH); 168.0, 170.1 (C=O). IR (cm⁻¹) 2988; 2857; 1740; 1655; 1516; 1345; 1243; 749; 698. mp. 181-184 °C.

Dimethyl (2R,6S)-1-(4-chlorobenzyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3,5-

dicarboxylate (14): C₂₈H₂₄N₃O₉Cl (582.0 g/mol), yield: 41 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.47 (s, 2H, NCH₂); 3.55 (s, 3H, COOCH₃); 3.58 (s, 3H, COOCH₃); 4.02 (d, 2H, ³J_{aa} = 10.8, CHCOOCH₃); 4.59 (d, 2H, ³J_{aa} = 10.8, NCH); 6.55-6.74 (m, 4H, CH_{Benzyl}); 7.49 (t, 2H, J = 7.3, H5'/5''); 7.78- 7.82 (m, 2H, H6'/6''); 8.09- 8.13 (m, 2H, H4'/4''); 8.35 (t, 2H, H2'/2''). ¹³C NMR (CDCl₃, δ = ppm) 52.7 (COOCH₃); 55.4 (NCH₂); 63.9 (CHC=O); 68.1 (NCH); 113.9, 123.7, 123.9, 128.8, 129.9, 133.2, (C2'/2'', C4'/4'', C5'/5'', C6'/6'', CH_{Benzyl}); 139.3 (Cq_{Benzyl}Cl); 140.8, 141.1, 148.3, 157.8 (Cq_{ar}); 166.6 (COOCH₃); 195.8 (C=O). IR (cm⁻¹) 3025; 2980; 1738; 1650; 1518; 1420; 1347; 1239; 880; 745; 697. mp. 144-146 °C.

Dimethyl (2R,6S)-1-(4-methoxybenzyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3,5-

dicarboxylate (15): C₂₉H₂₇N₃O₁₀ (577.5 g/mol), yield: 29 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 3.49 (s, 2H, NCH₂); 3.56 (s, 6H, COOCH₃); 3.71 (s, 3H, OCH₃); 4.01 (d, 2H, ³J_{aa} = 11.1, CHC=O); 4.56 (d, 2H, ³J_{aa} = 11.1, NCH); 6.57-6.62 (m, 4H, CH_{Benzyl}); 7.52 (t, 2H, J = 7.6, H5'/5''); 7.84 (m, 2H, H6'/6''); 8.12 (m, 2H, H2'/2'' or H4'/4''); 8.36 (s, 2H,

H4'/4'' or *H2'/2''*). ^{13}C NMR (CDCl_3 , δ = ppm) 52.6 (COOCH_3); 54.4 (NCH_2); 55.4 (OCH_3); 63.9 ($\text{CHC}=\text{O}$); 67.5 (NCH); 113.8, 123.8, 123.9, 129.8, 129.9, 135.0, (*C2'/2''*, *C4'/4''*, *C5'/5''*, *C6'/6''*, $\text{CH}_{\text{Benzyl}}$); 137.3 ($\text{Cq}_{\text{Benzyl}}\text{CH}_3$); 141.1, 141.4, 148.5, 158.8 (Cq_{ar}); 166.6 (COOCH_3); 195.6 ($\text{C}=\text{O}$). IR (cm^{-1}) 3536; 3088; 2957; 1732; 1524; 1436; 1352; 1248; 1172; 813; 741; 694. mp. 159-161 °C.

Dimethyl (2*R*,6*S*)-1-(4-methylbenzyl)-2,6-bis(3-nitrophenyl)-4-oxopiperidine 3,5-dicarboxylate (16): $\text{C}_{29}\text{H}_{27}\text{N}_3\text{O}_9$ (561.6 g/mol), yield: 41 %; ^1H NMR (CDCl_3 , δ = ppm, J = Hz) 2.19 (s, 3H, CqCH_3); 3.52 (s, 2H, NCH_2); 3.56 (s, 6H, COOCH_3); 4.07 (d, 2H, $^3J_{\text{aa}} = 11.1$, $\text{CHC}=\text{O}$); 4.57 (d, 2H, $^3J_{\text{aa}} = 11.1$, NCH); 6.57 (d, 2H, $J = 7.8$, *H3'/5'*); 6.84 (d, 2H, $J = 7.8$, *H2'/6'*); 7.50 (t, 2H, $J = 7.1$, *H5'/5''*); 7.87 (m, 2H, *H6'/6''*); 8.08-8.15 (m, 2H, *H2'/2''* or *H4'/4''*); 8.34 (s, 2H, *H4'/4''* or *H2'/2''*). ^{13}C NMR (CDCl_3 , δ = ppm) 20.9 (CH_3); 52.7 (OCH_3); 55.0 (NCH_2); 63.8 ($\text{CHC}=\text{O}$); 67.9 (NCH); 123.9, 124.0 (*C2'/2''/C4'/4''*); 128.4, 129.1 ($\text{CH}_{\text{Benzyl}}$); 129.9 (*C5'/5''*); 135.1 ($\text{CH}_2\text{Cq}_{\text{Benzyl}}$, *C6'/6''*); 137.3 ($\text{Cq}_{\text{Benzyl}}\text{CH}_3$); 141.1 (*C1'/1''*); 148.5 (*C3'/3''*); 166.6 (COOCH_3); 195.5 ($\text{C}=\text{O}$). IR (cm^{-1}) 2956; 1732; 1530; 1437; 1350; 1259; 1171; 810; 736; 695. mp. 170-172 °C.

Dimethyl (2*R*,6*S*)-1-benzyl-2,6-bis(3-nitrophenyl)-4-oxopiperidine-3,5-dicarboxylate (17): $\text{C}_{28}\text{H}_{25}\text{N}_3\text{O}_9$ (547.5 g/mol), yield: 15 %; ^1H NMR (CDCl_3 , δ = ppm, J = Hz) 3.52 (s, 2H, NCH_2); 3.57 (s, 6H, COOCH_3); 4.01 (d, 2H, $^3J_{\text{aa}} = 10.9$, CHCOOCH_3); 4.55 (d, 2H, $^3J_{\text{aa}} = 10.9$, NCH); 6.65-6.72 (m, 2H, $\text{CH}_{\text{Benzyl}}$); 6.98-7.02 (m, 3H, $\text{CH}_{\text{Benzyl}}$); 7.47 (t, 2H, $J = 8.0$, *H5'/5''*); 7.76-7.81 (m, 2H, *H6'/6''*); 8.06-8.10 (m, 2H, *H2'/2''* or *H4'/4''*); 8.34 (t, 2H, $J = 1.9$, *H4'/4''* or *H2'/2''*). ^{13}C NMR (CDCl_3 , δ = ppm) 52.6 (COOCH_3); 55.6 (CH_2); 63.9 ($\text{CHC}=\text{O}$); 68.3 (NCH); 123.8, 123.9 (*C2'/2''/C4'/4''*); 127.1, 128.2, 128.3 ($\text{CH}_{\text{Benzyl}}$); 129.8 (*C5'/5''*); 135.1 (*C6'/6''*); 137.0 ($\text{Cq}_{\text{Benzyl}}$); 141.3 (*C1'/1''*); 148.4 (*C3'/3''*); 166.6 (COOCH_3); 195.7 ($\text{C}=\text{O}$). IR (cm^{-1}) 2953; 1748; 1528; 1441; 1348; 1242; 805; 741; 693. mp. 144-146 °C.

Dimethyl (2*R*,6*S*)-1-allyl-4-oxo-2,6-diphenylpiperidine-3,5-dicarboxylate (18): $\text{C}_{24}\text{H}_{25}\text{NO}_5$ (407.5 g/mol), yield: 81 %; keto-enol ratio: 4:3, ^1H NMR (CDCl_3 , δ = ppm, J = Hz), 2.79-2.86 (m, 4H, $\text{NCH}_2\text{CH}=\text{CH}_2$, ketone, $\text{NCH}_2\text{CH}=\text{CH}_2$, enol); 3.53 (s, 6H, COOCH_3 , ketone); 3.64, 3.68 (2s, each 3H, COOCH_3 , enol); 3.81-3.90 (m, 2H, $\text{CHC}=\text{O}$, ketone); 3.94 (d, 1H, $^3J_{\text{aa}} = 10.1$, $\text{CHC}-\text{OH}$, enol); 4.35-4.45 (m, 3H, NCH , ketone, NCHCH , enol); 4.59-4.66 (m, 1H, $\text{NCH}_2\text{CH}=\text{CH}_2$, ketone); 4.84 (s, 1H, NCHCq , enol);

5.06-5.19 (m, 3H, NCH₂CH=CH₂, ketone, NCH₂CH=CH₂, enol); 5.67-5.87 (m, 2H, NCH₂CH=CH₂, ketone, NCH₂CH=CH₂, enol); 7.20-7.49 (m, 20H, CH_{ar}, ketone, CH_{ar}, enol); 12.45 (OH, enol). ¹³C NMR (CDCl₃, δ = ppm) 46.8 (CHC-OH, enol); 49.6, 50.9 (NCH₂CH=CH₂, ketone and enol); 52.0, 52.7 (COOCH₃, enol); 52.2 (COOCH₃, ketone); 57.8, 57.9 (NCH, ketone); 64.9, 66.3 (NCH, enol); 99.0 (C=C-OH, enol); 117.7 (NCH₂CH=CH₂, ketone); 120.5 (NCH₂CH=CH₂, enol); 127.2, 127.8, 128.1, 128.2, 128.4, 128.5, 128.5, 128.9, 129.2, 130.1 (NCH₂CH=CH₂, enol and CH_{ar}, ketone and enol); 136.8 (NCH₂CH=CH₂, ketone); 138.8, 139.5, 141.8 (C_q_{ar}, ketone and enol); 167.4 (C=C-OH, enol and COOCH₃, ketone); 171.1, 172.3 (C=O, enol); 197.5 (C=O, ketone). IR (cm⁻¹) 2951; 2847; 1738; 1653; 1438; 1273; 1209; 764; 698. mp. 142 °C.

Dimethyl (2*R*,6*S*)-4,4-dihydroxy-2,6-dimethyl-piperidinium-3,5-dicarboxylate

hydrobromide (30a): C₁₁H₂₀NO₆Br (342.2 g/mol), yield: 62 %; ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) 1.16 (d, 6H, J = 6.6, CHCH₃); 2.81 (d, 2H, ³J_{aa} = 11.6, CHCOOCH₃); 3.57 (m, 2H, CHCH₃); 3.67 (s, 6H, COOCH₃); 5.70, 6.43 (2s, each 1H, OH); 8.83, 9.17 (2s, each 1H, NH₂⁺). ¹³C NMR (DMSO-d₆, δ = ppm) 16.4 (CHCH₃); 50.4 (CHCH₃); 52.1 (COOCH₃); 55.9 (CHCOOCH₃); 92.3 (HO-C-OH); 168.7 (C=O). IR (cm⁻¹) 3489; 2943; 2888; 2780; 2736; 2477; 1744; 1719; 1383; 1221; 1024. mp. 178-182 °C.

Dimethyl (2*RS*,6*RS*)-4-hydroxy-2,6-diethyl-piperidine-3,5-dicarboxylate (30b):

C₁₃H₂₁NO₅ (271.3 g/mol), yield: 97 % (oil); keto-enol ratio: 1:2. ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.84 (t, 3H, J = 7.6, CHCH₂CH₃, enol); 0.93 (t, 3H, J = 7.5, CHCH₂CH₃, enol); 0.94 (t, 3H, J = 7.3, CHCH₂CH₃, ketone); 0.96 (t, 3H, J = 7.3, CHCH₂CH₃, ketone); 1.24-1.66 (m, 7H, CH₂CH₃, ketone, CH₂CH₃, enol); 1.74-1.85 (m, 1H, CH₂CH₃, enol); 2.61-2.68 (m, 1H, CHCH₂CH₃, enol); 2.84-2.89, 3.06-3.13 (2m, each 1H, CHCH₂CH₃, ketone); 3.22 (dd, 1H, ³J_{ae} = 3.8, ³J = 1.5, CHCOOCH₃, enol); 3.43 (d, 1H, ³J_{ae} = 3.3, CHCOOCH₃, ketone); 3.58-3.64 (m, 2H, CHCH₂CH₃, enol, CHCOOCH₃, ketone); 3.64, 3.68 (2s, each 3H, COOCH₃, ketone); 3.67, 3.72 (2s, each 3H, COOCH₃, enol); 11.9 (brs, 1H, OH). ¹³C NMR (CDCl₃, δ = ppm) 9.3 (CHCH₂CH₃, enol); 9.9 (CHCH₂CH₃, ketone); 11.0 (CHCH₂CH₃, enol and CHCH₂CH₃, ketone); 26.6, 27.9 (CHCH₂CH₃, enol); 26.8, 28.3 (CHCH₂CH₃, ketone); 48.3 (CHCOOCH₃, enol); 51.6, 52.2 (COOCH₃, enol); 52.0, 52.3 (COOCH₃, ketone); 53.5 (CqCHCH₂CH₃, enol); 56.2

(CHCHCH₂CH₃, enol); 60.7, 61.5 (CHCOOCH₃, ketone); 60.9, 62.2 (CHCH₂CH₃, ketone); 103.4 (Cq=C-OH); 166.9 (Cq=C-OH, enol); 168.5, 169.8 (COOCH₃, ketone); 170.8, 172.3 (COOCH₃, enol); 200.5 (C=O, ketone).

Dimethyl (2*RS*,6*RS*)-4-hydroxy-2,6-dipropyl-piperidinium-3,5-dicarboxylate

hydrobromide (30c): C₁₅H₂₆NO₅Br (380.3 g/mol), yield: 50 %. ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.96 (t, 3H, J = 7.2, CqCHCH₂CH₂CH₃); 0.98 (t, 3H, J = 7.2, CHCHCH₂CH₂CH₃); 1.28-1.73 (m, 4H, CH₂CH₂CH₃ and 1H, CHCHCH₂CH₂CH₃); 1.93-2.19 (m, 2H, CqCHCH₂CH₂CH₃); 2.45-2.57 (m, 1H, CHCHCH₂CH₂CH₃); 3.42-3.52 (m, 1H, CHCHCH₂CH₂CH₃); 3.52-3.57 (d, 1H, ³J_{ae} = 2.8, CHCOOCH₃); 3.84 (s, 3H, CqCOOCH₃); 3.89 (s, 3H, CHCOOCH₃); 4.57-4.67 (m, 1H, CqCHCH₂CH₂CH₃); 7.86, 11.45 (2s, each 1H, NH₂⁺); 12.23 (s, 1H, OH). ¹³C NMR (CDCl₃, δ = ppm) 13.6, 14.0 (CH₂CH₃); 17.2, 18.8 (CH₂CH₃); 31.4, 34.8 (CH₂CH₂CH₃); 45.5 (CHCOOCH₃); 52.7 (CqCOOCH₃); 52.9 (CqCHCH₂CH₃); 52.6 (CHCOOCH₃); 53.5 (CHCHCH₂CH₃); 98.9 (Cq=C-OH); 164.6 (Cq=C-OH); 169.1 (CHCOOCH₃); 169.8 (CqCOOCH₃). IR (cm⁻¹) 3064; 2958, 2933; 2756; 2633; 1747; 1678; 1630; 1533; 1437. mp. 142-143 °C.

Dimethyl (2*RS*,6*RS*)-4-hydroxy -2,6-dibutyl-3,5-piperidinium-dicarboxylate

hydrobromide (30d): C₁₇H₃₀NO₅Br (408.3 g/mol), yield: 24 %. ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.91 (t, 6H, J = 7.2, CHCH₂CH₂CH₃); 1.19-1.63, 1.97-2.19 and 2.55-2.66 (3m, 12H, CHCH₂CH₂CH₂CH₃); 3.39-3.49 (m, 1H, CHCHCH₂CH₂CH₂CH₃); 3.54-3.58 (d, 1H, ³J_{ae} = 3.3, CHCOOCH₃); 3.85 (s, 3H, CqCOOCH₃); 3.90 (s, 3H, CHCOOCH₃); 4.58-4.71 (m, 1H, CqCHCH₂CH₂CH₃); 6.52, 11.85 (2s, each 1H, NH₂⁺); 12.27 (s, 1H, OH). ¹³C NMR (CDCl₃, δ = ppm) 13.8, 13.9 (CH₂CH₃); 22.1, 22.4 (CH₂CH₃); 25.4, 27.5 (CH₂CH₂CH₃); 29.2, 32.3 (CH₂CH₂CH₂CH₃); 44.8 (CHCOOCH₃); 52.8 (CqCOOCH₃); 52.9 (CqCHCH₂CH₂CH₂CH₃); 54.2 (CHCOOCH₃); 54.5 (CHCHCH₂CH₂CH₂CH₃); 98.5 (Cq=C-OH); 164.1 (Cq=C-OH); 170.1 (CHCOOCH₃); 170.3 (CqCOOCH₃). IR (cm⁻¹) 3080; 2957; 2929; 2864; 2638; 1748; 1666; 1630; 1534; 1440. mp. 144-146 °C.

(2*R*,6*S*)-2,6-Dimethyl-4-oxopiperidinium chloride (31a): C₇H₁₂NOCl (163.7 g/mol), yield: 95 %. ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) 1.36 (d, 6H, J = 6.3, CHCH₃); 2.44 (dd, 2H, ²J = 15.4, ³J_{ae} = 2.8, CH₂); 2.62 (dd, 2H, ²J = 15.4, ³J_{aa} = 12.9, CH₂); 3.61 (m, 2H, CH); 9.38, 9.46 (2s, each 1H, NH₂⁺). ¹³C NMR (DMSO-d₆, δ = ppm) 18.5 (CHCH₃);

44.2 (CH₂); 50.8 (CH); 202.9 (C=O). IR (cm⁻¹) 2929; 2781; 2723; 2665; 2569; 1726; 1666; 1579; 1451; 1406. mp.: 227-229 °C.

(2R,6S)/(2RS,6RS)-2,6-Diethyl-4-oxopiperidinium chloride (31b): C₉H₁₈NOCl (191.7 g/mol), yield: 93 %; *cis*-/*trans* ratio: 5:1 ¹H NMR (DMSO, δ = ppm, J = Hz) *cis*-isomer: 0.92 (t, 6H, CH₂CH₃, J = 7.6); 1.43-1.98 (m, 4H, CH₂CH₃); 2.45-2.63 (m, 4H, CH₂C=O); 3.54-3.57 (m, CHCH₂CH₃); 8.87-9.23 (m, 2H, NH₂⁺), *trans*-isomer: 0.92 (t, 6H, J = 7.5, CH₂CH₃); 1.43-1.98 (m, 4H, CH₂CH₃); 2.45-2.63 (m, 2H, CH₂C=O); 2.72 (dd, 2H²J = 15.3, ³J_{ae} = 4.7, CH₂C=O); 3.61-3.67 (m, CHCH₂CH₃); 9.23-9.32 (m, 2H, NH₂⁺). ¹³C NMR (DMSO, δ = ppm) *cis*-isomer: 9.2 (CH₂CH₃); 25.4 (CH₂CH₃); 41.8 (CH₂C=O); 56.1 (CHCH₂CH₃); 202.9 (C=O), *trans*-isomer: 9.5 (CH₂CH₃); 24.3 (CH₂CH₃); 41.5 (CH₂C=O); 52.9 (CHCH₂CH₃); 203.5 (C=O). IR (cm⁻¹) 2929; 2781, 2723; 2665; 2569; 1726; 1666; 1579; 1451; 1406. mp. 181-183 °C.

(2R,6S)-/ (2RS,6RS)-2,6-Dipropyl-4-oxopiperidinium chloride (31c): C₁₁H₂₂NOCl (219.8 g/mol), yield: 92 %; *cis*-/*trans* ratio: 4:1 ¹H NMR (DMSO, δ = ppm, J = Hz), *cis*-isomer: 0.88 (t, 6H, J = 7.3, CH₂CH₃); 1.21-1.90 (m, 8H, CH₂CH₂CH₃); 2.42-2.52 (m, 2H, CH₂C=O); 2.61 (dd, 2H, ²J = 15.3, ³J_{aa} = 12.8, CH₂C=O); 3.54-3.65 (m, CHCH₂CH₂CH₃); 8.88-9.35 (m, 2H, NH₂⁺), *trans*-isomer: 0.88 (t, 6H, J = 7.3, CH₂CH₃); 1.21-1.90 (m, 4H, CH₂CH₂CH₃); 2.42-2.52 (m, 2H, CH₂C=O); 2.72 (dd, 2H, ²J = 15.4, ³J_{ae} = 4.8, CH₂C=O); 3.61-3.78 (m, CHCH₂CH₃); 9.35-9.48 (m, 2H, NH₂⁺). ¹³C NMR (DMSO, δ = ppm) *cis*-isomer: 13.5 (CH₂CH₃); 17.5 (CH₂CH₃); 34.3 (CH₂CH₂CH₃); 42.2 (CH₂C=O); 54.4 (CHCH₂CH₃); 202.8 (C=O), *trans*-isomer: 13.6 (CH₂CH₃); 17.9 (CH₂CH₃); 33.2 (CH₂CH₂CH₃); 41.9 (CH₂C=O); 51.4 (CHCH₂CH₃); 203.5 (C=O). IR (cm⁻¹) 2929; 2791; 1726; 1596; 1408. mp. 194 °C.

(2R,6S)-/ (2RS,6RS)-2,6-Dibutyl-4-oxopiperidinium chloride (31d): C₁₃H₂₆NOCl (247.9 g/mol), yield: 90 %; *cis*-/*trans* ratio: 2:1 ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) *cis*-isomer: 0.88 (t, 6H, J = 6.8, CH₂CH₃); 1.19-1.97 (m, 12H, CH₂CH₂CH₂CH₃); 2.44-2.52 (m, 2H, CH₂C=O); 2.59 (dd, 2H, ²J = 15.3, ³J_{aa} = 12.8, CH₂C=O); 3.47-3.61 (m, CHCH₂CH₂CH₂CH₃); 8.92-9.39 (m, 2H, NH₂⁺), *trans*-isomer: 0.87 (t, 6H, J = 6.7, CH₂CH₃); 1.19-1.97 (m, 12H, CH₂CH₂CH₂CH₃); 2.44-2.52 (m, 2H, CH₂C=O); 2.71 (dd, 2H, ²J = 15.3, ³J_{ae} = 4.7, CH₂C=O); 3.65-3.72 (m, CHCH₂CH₂CH₂CH₃); 9.39-9.50 (m, 2H, NH₂⁺). ¹³C NMR (DMSO-d₆, δ = ppm) *cis*-isomer: 13.6 (CH₂CH₃); 21.7, 26.1, 32.0

(CH₂CH₂CH₂CH₃); 42.3 (CH₂C=O); 54.7 (CHCH₂CH₂CH₂CH₃); 202.8 (C=O), *trans*-isomer: 13.6 (CH₂CH₃); 21.7, 26.5, 30.8 (CH₂CH₂CH₂CH₃); 41.9 (CH₂C=O); 51.5 (CHCH₂CH₂CH₂CH₃); 203.5 (C=O). IR (cm⁻¹) 2928; 2780, 2723; 1726; 1664; 1579; 1448; 1406. mp. 212 °C.

(2R,6S)-2,6-Dimethyl-4-phenylamino-piperidine-4-carbonitrile (32a): C₁₄H₁₉N₃ (229.3 g/mol), yield: 71 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.16 (d, 6H, J = 6.3, CH₃); 1.27 (dd, 2H, ²J = 12.6, ³J_{aa} = 11.6, CH₂); 1.57 (brs, NH); 2.36 (d, 2H, ²J = 12.6, CH₂); 3.08-3.18 (m, 2H, CH); 3.62 (s, 1H, NH); 6.89-6.97 (t, 3H, J = 8.1, CH_{ar}); 7.22-7.29 (m, 2H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 22.0 (CH₃); 44.2 (CH₂); 48.6 (CH); 54.7 (C-CN); 121.1 (CN); 118.3, 121.2, 129.4 (CH_{ar}); 143.4 (C_{qar}). IR (cm⁻¹) 3368; 3304; 2965; 2928; 2874; 2228; 1602; 1499; 1317; 1163; 752; 695. mp. 126 – 128 °C.

(2R,6S)-4-Benzylamino-2,6-dimethylpiperidine-4-carbonitrile (32b): C₁₅H₂₁N₃ (243.4 g/mol), yield: 68 % (oil); ratio of rotamers: 4:1. ¹H NMR (CDCl₃, δ = ppm, J = Hz) isomer A: 1.13 (t, 6H, J = 6.1, CHCH₃); 1.22 (dd, 2H, ²J = 12.6, ³J_{aa} = 11.6, CH₂-Cq); 2.02 (d, 2H, ²J = 12.6, CH₂-Cq); 3.01-3.11 (m, 2H, CH); 3.91 (s, 2H, NHCH₂); 7.24-7.38 (m, 5H, CH_{ar}), isomer B: 1.04 (t, 6H, J = 6.3, CH₂CH₃); 1.53 (dd, 2H, ²J = 13.9, ³J_{aa} = 10.9, CH₂-Cq); 1.94 (d, 2H, ²J = 13.9, CH₂-Cq); 3.15-3.25 (m, 2H, CH); 3.85 (s, 2H, NHCH₂); 7.24-7.38 (m, 5H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) isomer A: 22.1 (CH₃); 43.6 (CH₂-Cq); 48.4 (NHCH₂); 48.6 (CH); 57.3 (Cq); 122.0 (CN); 127.5, 128.4, 128.6 (CH_{ar}); 139.2 (C_{qar}), isomer B: 22.1 (CH₃); 42.1 (CH₂-Cq); 48.8 (NHCH₂); 45.5 (CH); 54.6 (Cq); 122.3 (CN); 127.5, 128.4, 128.6 (CH_{ar}); 139.3 (C_{qar}). IR (cm⁻¹) 3311; 2962; 2927; 2841; 2218; 1454; 1376; 1318; 1159; 739; 701. mp. 126-128 °C.

(2R,6S)-2,6-Diethyl-4-phenylamino-piperidine-4-carbonitrile (32c): C₁₆H₂₃N₃ (257.4 g/mol), yield: 52 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.98 (t, 6H, J = 7.6, CH₃); 1.51-1.71 (m, 6H, CH₂CH₃, Cq-CH₂); 2.44-2.50 (d, 2H, ²J = 13.1, Cq-CH₂); 2.95-3.06 (m, 2H, CH); 6.91-6.98 (m, 3H, CH_{ar}); 7.23-7.28 (m, 2H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 10.2 (CH₃); 27.7 (CH₂); 40.7 (CH₂); 54.2 (CH); 55.2 (Cq); 120.7 (CN); 118.2, 121.3, 129.5 (CH_{ar}); 143.4 (C_{qar}). IR (cm⁻¹) 3258; 2971; 2940; 2225; 1603; 1557; 1497; 1404; 1319; 1258; 748; 695. mp. 142-143 °C.

(2R,6S)-4-Benzylamino-2,6-diethylpiperidine-4-carbonitrile (32d): C₁₇H₂₅N₃ (271.4 g/mol), yield: 47 %; ratio of rotamers: 5:1. ¹H NMR (CDCl₃, δ = ppm, J = Hz) isomer A: 0.96 (t, 6H, J = 7.5, CH₂CH₃); 1.20 (dd, 2H, ²J = 12.9, ³J_{aa} = 11.6, CH₂-Cq); 1.34-1.58 (m, 4H, CH₂CH₃); 2.09 (d, 2H, ²J = 12.9, CH₂Cq); 2.78-2.87 (m, 2H, CH); 3.94 (s, 2H, CH₂NH); 7.26-7.39 (m, 5H, CH_{ar}), isomer B: 0.88 (t, 6H, J = 7.5, CH₂CH₃); 1.63 (dd, 2H, ²J = 13.6, ³J_{aa} = 11.6, CH₂-Cq); 1.34-1.58 (m, 4H, CH₂CH₃); 2.04 (d, 2H, ²J = 13.6, CH₂ Cq); 2.97-3.03 (m, 2H, CH); 3.87 (s, 2H, NHCH₂); 7.26-7.39 (m, 5H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) isomer A: 10.3 (CH₃); 29.1 (CH₂CH₃); 41.9 (CH₂ Cq); 48.6 (NHCH₂); 54.7 (CH); 57.4 (Cq); 122.0 (CN); 127.6, 128.5, 128.7 (CH_{ar}); 139.2 (Cq_{ar}), isomer B: 10.2 (CH₃); 28.8 (CH₂CH₃); 40.0 (CH₂ Cq); 49.0 (NHCH₂); 51.6 (CH); 54.5 (Cq); 122.3 (CN); 127.7, 128.6, 128.7 (CH_{ar}); 139.3 (Cq_{ar}). IR (cm⁻¹) 3304; 3237; 2963; 2923; 2877; 2218; 1558; 1456; 1381; 1329; 1142; 1093; 740; 699. mp. 109-111 °C.

(2R,6S)-4-Phenylamino-2,6-dipropylpiperidine-4-carbonitrile (32e): C₁₈H₂₇N₃ (285.4 g/mol), yield: 27 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.89 (t, 6H, J = 6.9, CH₃); 1.16 (dd, 2H, ²J = 12.5, ³J_{aa} = 12.0, CqCH₂); 1.30-1.42 (m, 8H, CH₂CH₂CH₃); 2.34 (d, 2H, ²J = 12.5, CqCH₂); 2.70-2.79 (m, 2H, CH); 6.72 (t, 1H, J = 7.3, CH_{ar}); 6.86 (d, 2H, J = 7.8, CH_{ar}); 7.16 (2t, each 1H, J = 7.7, J = 7.6, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 14.1 (CH₃); 18.4, 37.8 (CH₂CH₂CH₃); 41.9 (CqCH₂); 52.3 (CH); 53.6 (Cq); 121.2 (CN); 115.7, 118.3, 128.8 (CH_{ar}); 144.8 (Cq_{ar}). IR (cm⁻¹) 3371; 2958; 2928; 2870; 2230; 1603; 1500; 1321; 1256; 1156; 751; 693. mp. 94 °C.

(2R,6S)-2,6-Dibutyl-4-phenylamino-piperidine-4-carbonitrile (32f): C₂₀H₃₁N₃ (313.5 g/mol), yield: 21 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.91 (t, 6H, J = 6.9, CH₃); 1.27-1.41, 1.56-1.91 (2m, 14H, CH₂CH₂CH₂CH₃, Cq-CH₂ axial); 2.48-2.55 (d, 2H, ²J = 12.9, Cq-CH₂ equatorial); 3.11-3.22 (m, 2H, CH); 6.92-6.99 (m, 3H, CH_{ar}); 7.24-7.29 (m, 2H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 14.1 (CH₃); 22.6 (CH₂); 27.9 (CH₂); 33.8 (CH₂); 40.6 (CH₂); 54.0 (CH); 54.2 (Cq); 120.4 (CN); 118.5, 121.6, 129.6 (CH_{ar}); 143.1 (Cq_{ar}). IR (cm⁻¹) 3370; 2958; 2928; 2870; 2230; 1603; 1500; 1321; 1257; 1156; 751; 694. mp. 79 °C.

(2R,6S)-7,9-Dimethyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (33):

C₁₅H₁₉N₃O₂ (273.3 g/mol), yield: 52 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.05 (d, 6H,

$J = 6.3$, CH_3); 1.33 (dd, 2H, $^2J = 12.5$, $^3J_{\text{aa}} = 12.3$, CH_2Cq); 1.87 (d, 2H, $^2J = 12.5$, CH_2Cq); 3.45-3.58 (m, 2H, CH); 7.15-7.19 (m, 2H, CH_{ar}); 7.41-7.47 (m, 3H, CH_{ar}). ^{13}C NMR (CDCl_3 , $\delta = \text{ppm}$) 22.3 (CH_3); 39.5 (CqCH_2); 46.6 (CH); 65.7 (Cq); 129.4, 129.8, 130.9 (CH_{ar}); 132.6 (Cq_{ar}); 154.9 (C=O); 176.2 (Cq-C=O). IR (cm^{-1}) 2978; 2942; 2716; 1716; 1410; 1386; 1152; 706; 629. mp. 256 °C.

(2R,6S)-1-Benzyl-7,9-diethyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (34):

$\text{C}_{18}\text{H}_{25}\text{N}_3\text{O}_2$ (315.4 g/mol), yield: 84 %; ratio of rotamers: 5:1 ^1H NMR (CDCl_3 , $\delta = \text{ppm}$, $J = \text{Hz}$) rotamere A: 0.86 (t, 6H, $J = 7.5$, CH_2CH_3); 1.13-1.78 (m, 4H, CH_2CH_3 , 4H, $\text{CH}_2\text{-Cq}$); 3.17-3.29 (m, 2H, CH); 4.51 (s, 2H); 7.20-7.36 (m, 5H, CH_{ar}), rotamere B: 0.64 (t, 6H, $J = 7.5$, CH_2CH_3); 1.13-1.78 (m, 4H, CH_2CH_3 , 4H, $\text{CH}_2\text{-Cq}$); 2.51-2.62 (m, 2H, CH); 4.87 (s, 2H, $\text{NCH}_2\text{Benzyl}$); 7.20-7.36 (m, 5H, CH_{ar}). ^{13}C NMR (CDCl_3 , $\delta = \text{ppm}$) rotamere A: 10.2 (CH_3); 29.5 (CH_2CH_3); 37.4 ($\text{CH}_2\text{-Cq}$); 42.0 (NH-CH_2); 52.4 (CH); 64.5 (Cq); 127.6, 127.6, 128.7 (CH_{ar}); 138.0 (Cq_{ar}); 155.0 (Cq-C=O); 179.8 (C=O), rotamere B: 9.9 (CH_3); 30.1 (CH_2CH_3); 38.8 ($\text{CH}_2\text{-Cq}$); 45.5 (NH-CH_2); 53.9 (CH); 65.9 (Cq); 129.9, 127.6, 128.8 (CH_{ar}); 137.8 (Cq_{ar}); 156.9 (Cq-C=O); 177.0 (C=O). IR (cm^{-1}) 3291; 2963; 2925; 2876; 1709; 1413; 1131; 703; 623. mp. 284-286 °C

(2R,6S)-1-Phenyl-7,9-dipropyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (35):

$\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_2$ (329.5 g/mol), yield: 66 %; ^1H NMR (DMSO , $\delta = \text{ppm}$, $J = \text{Hz}$) 0.84 (t, 6H, $J = 7.1$, CH_3); 1.17-1.32 (m, 10H, $\text{CH}_2\text{CH}_2\text{CH}_3$, CqCH_2); 1.78-1.89 (m, 2H, CqCH_2); 3.21-3.33 (m, 2H, CH); 6.96-7.14 (m, 2H, CH_{ar}); 7.33-7.54 (m, 3H, CH_{ar}). ^{13}C NMR (DMSO , $\delta = \text{ppm}$) 14.3 (CH_3), 19.1 ($\text{CH}_2\text{CH}_2\text{CH}_3$); 38.6 ($\text{CH}_2\text{CH}_2\text{CH}_3$); 39.2 (CqCH_2); 50.7 (CH); 65.9 (Cq); 129.3, 129.8, 130.9 (CH_{ar}); 132.6 (Cq_{ar}); 154.7 (Cq-C=O); 176.1 (NC=ON). IR (cm^{-1}) 3270; 2961; 2924; 2871; 1709; 1387; 1152; 700; 625. mp. 216-218 °C.

(2R,6S)-7,9-Dibutyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (36):

$\text{C}_{21}\text{H}_{31}\text{N}_3\text{O}_2$ (357.5 g/mol), yield: 42 %; ^1H NMR (DMSO , $\delta = \text{ppm}$, $J = \text{Hz}$) 0.87 (t, 6H, $J = 6.8$, CH_2CH_3); 1.18-1.40 and 1.74-1.86 (2m, 12H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); 1.54 (dd, 2H, $^2J = 13.9$, $^3J_{\text{aa}} = 12.4$, $\text{CH}_2\text{-Cq}$); 2.41 (d, 2H, $^2J = 13.9$, $\text{CH}_2\text{-Cq}$); 3.53-3.65 (m, 2H, CH); 7.30-7.36 (m, 2H, CH_{ar}); 7.42-7.53 (m, 2H, CH_{ar}). ^{13}C NMR (DMSO , $\delta = \text{ppm}$) 13.7 (CH_3); 21.7 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); 26.5 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); 31.9 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); 33.1 ($\text{CH}_2\text{-Cq}$); 51.5 (CH); 62.0 (Cq); 128.7, 129.4, 131.0 (CH_{ar}); 133.0 (Cq_{ar}); 154.7 (Cq-

C=O); 176.1 (NC=ON). **IR** (cm⁻¹) 3502; 3387; 2957; 2932; 2862; 2726; 1715; 1397; 1150; 705; 625. mp. 305 °C.

(2R,6S)-8-Benzyl-7,9-diethyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (44):

C₂₄H₂₉N₃O₂ (391.5 g/mol), yield: 59 %; ¹H NMR (DMSO, δ = ppm, J = Hz) 0.70 (t, 6H, J = 7.3, CH₂CH₃); 0.95-1.07 (m, 2H, CH₂CH₃); 1.31-1.46 (m, 2H, CH₂-Cq axial, 2H, CH₂CH₃); 1.68 (d, 2H, ²J = 12.6, CH₂-Cq äquatorial); 3.32-3.42 (m, 2H, NCH₂, 2H, CH); 7.09 (t, 1H, J = 7.2, CH_{ar}); 7.20 (t, 2H, J = 7.5, CH_{ar}); 7.26 (t, 4H, J = 8.0, CH_{ar}); 7.35 (t, 1H, J = 7.3, CH_{ar}); 7.45 (t, 2H, J = 7.6, CH_{ar}). ¹³C NMR (DMSO, δ = ppm) 10.9 (CH₃); 27.3 (CH₂CH₃); 32.6 (CH₂-Cq); 47.7 (NCH₂); 59.1 (CH); 63.9 (Cq); 125.7, 127.1, 127.7, 128.9, 130.1, (CH_{ar}); 136.0, 143.4 (Cq_{ar}); 157.7 (C=O); 183.5 (Cq-C=O). **IR** (cm⁻¹) 2963; 2930; 2865; 1734; 1603; 1494; 1367; 1135; 727; 696. mp. 294-295 °C.

(2R,6S)-1-Benzyl-3-(2-hydroxy-ethyl)-7,9-dimethyl-1,3,8-triaza-spiro[4.5]decane-

2,4-dione (37): C₁₈H₂₅N₃O₃ (331.4 g/mol), yield: 48 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.06 (d, 6H, J = 6.3, CH₃); 1.48 (dd, 2H, ²J = 13.3, ³J_{aa} = 11.0, CqCH₂); 1.59 (dd, 2H, ²J = 13.3, ³J_{ae} = 1.9, CqCH₂); 3.46-3.56 (m, 2H, CHCH₃); 3.74-3.78 (m, 2H, NCH₂CH₂OH); 3.80-3.84 (m, 2H, NCH₂CH₂OH); 4.53 (s, 2H, NCH₂); 7.25-7.32 (m, 5H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 22.2 (CH₃); 38.8 (CqCH₂); 41.9 (CH₂CH₂OH); 42.4 (NCH₂); 46.7 (NCH); 61.2 (CH₂CH₂OH); 63.5 (Cq); 127.5, 127.7, 128.8 (CH_{ar}); 156.6 (NC=ON); 176.4 (CqC=O). **IR** (cm⁻¹) 3302; 2963; 2934; 2853; 1695; 1447; 1048; 700. mp. 195-196 °C.

(2R,6S)-3-Benzyl-7,9-diethyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (38):

C₂₄H₂₉N₃O₂ (391.5 g/mol), yield: 55 %; ratio of rotamers: 6:1. ¹H NMR (CDCl₃, δ = ppm, J = Hz) rotamer A: 0.90 (t, 6H, J = 7.5, CH₂CH₃); 1.20-1.45 (m, 6H, CH₂-Cq axial, CH₂CH₃); 1.82 (d, 2H, ²J = 12.6, CH₂-Cq äquatorial); 3.25-3.35 (m, 2H, CH); 4.73 (s, 2H, CH₂ Benzyl); 7.12-7.48 (m, 10H, CH_{ar}), rotamer B: 0.81 (t, 6H, J = 7.5, CH₂CH₃); 1.20-1.45 (4H, CH₂CH₃); 1.73-1.79 (m, 2H, CH₂-Cq axial); 1.97 (d, 2H, ²J = 13.9, CH₂-Cq äquatorial); 2.22-2.31 (m, 2H, CH); 4.73 (s, 2H, CH₂ Benzyl); 7.12-7.48 (m, 10H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) rotamer A: 10.3 (CH₃); 29.4 (CH₂CH₃); 38.0 (CH₂-Cq); 42.4 (CH₂ Benzyl); 52.7 (CH); 64.3 (Cq); 127.9; 128.7; 128.8; 129.1, 129.7, 130.8 (CH_{ar}); 132.9 (N-Cq_{ar}); 136.3 (CH₂-Cq_{ar}); 155.0 (NC=ON); 175.3 (Cq-C=O), rotamer B:

10.1 (CH₃); 30.0 (CH₂CH₃); 39.3 (CH₂-Cq); 43.0 (CH₂ Benzyl); 52.9 (CH); 65.6 (Cq); 127.3; 128.0; 128.6; 129.4, 129.6, 131.0 (CH_{ar}); 136.2 (N-Cq_{ar}); 136.5 (CH₂-Cq_{ar}); 155.5 (NC=ON); 175.5 (Cq-C=O). IR (cm⁻¹) 2962; 2933; 1704; 1434; 1412; 1152; 743; 697. mp. 74-75 °C.

(2R,6S)-1-Benzyl-7,9-dimethyl-3-(4-nitro-benzyl)-1,3,8-triaza-spiro[4.5]decane-2,4-dione (39): C₂₃H₂₆N₄O₄ (422.5 g/mol), yield: 71 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 1.11 (d, 6H, J = 6.3, CH₃); 1.45 (d, 2H, ²J = 12.4, CH₂ Cq æquatorial); 1.80 (dd, 2H, ²J = 12.4, ³J_{aa} = 12.9, CH₂Cq); 3.52-3.62 (m, 2H, CH); 4.50 (s, 2H, CH₂ Benzyl); 4.70 (s, 2H, CH₂ 4-Nitrobenzyl); 7.17-7.31 (m, 5H, CH_{Benzyl}); 7.46-7.51 (m, 2H, CH_{4-Nitrobenzyl}); 8.11-8.17 (m, 2H, CH_{4-Nitrobenzyl}). ¹³C NMR (CDCl₃, δ = ppm) 20.6 (CH₃); 37.1 (CHCH₂); 41.7 (CH₂ 4-Nitrobenzyl); 42.6 (CH₂ Benzyl); 47.5 (CH); 62.7 (Cq); 124.2, 127.9, 127.9, 128.9, 129.5 (CH_{ar}); 137.6 (CH₂-Cq_{Benzyl}); 143.1 (CH₂-Cq_{4-Nitrobenzyl}); 147.9 (Cq-NO₂); 155.3 (NC=ON); 175.1 (Cq-C=O). IR (cm⁻¹) 2974; 2934; 1708; 1575; 1518; 1439; 1413; 1343; 703; 646. mp. 161-162 °C.

(2R,6S)-7,9-Diethyl-3-phenethyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (40): C₂₅H₃₁N₃O₂ (405.5 g/mol), yield: 62 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.87 (t, 6H, J = 7.6, CH₂CH₃); 1.15-1.32 (m, 6H, CH₂-Cq axial, CH₂CH₃); 1.59 (d, 2H, ²J = 12.4, CH₂-Cq æquatorial); 3.03 (t, 2H, NCH₂CH₂); 3.09-3.18 (m, 2H, CH); 3.85 (t, 2H, NCH₂CH₂); 4.73 (s, 1H, NH); 7.05-7.44 (m, 10H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 10.4 (CH₃); 29.8 (CH₂CH₃); 33.7 (NCH₂CH₂); 38.2 (CH₂-Cq); 39.3 (NCH₂CH₂); 52.4 (CH); 64.2 (Cq); 126.8; 128.5; 129.0; 129.3, 129.7, 130.8 (CH_{ar}); 133.0 (N-Cq_{ar}); 138.0 (CH₂-Cq_{ar}); 155.1 (NC=ON); 175.5 (Cq-C=O). IR (cm⁻¹) 2934; 2857; 1700; 1443; 1415; 1128; 739; 699; 623. mp. 146-147 °C.

(2R,6S)-7,9-Diethyl-1-phenyl-3-(3-phenyl-propyl)-1,3,8-triaza-spiro[4.5]decane-2,4-dione (41): C₂₆H₃₃N₃O₂ (419.6 g/mol), yield: 63 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.91 (t, 6H, J = 7.5, CH₂CH₃); 1.24-1.38 (m, 6H, CH₂-Cq axial, CH₂CH₃); 1.75 (d, 2H, ²J = 12.1, CH₂-Cq æquatorial); 2.05 (quin, 2H, J = 7.5, NCH₂CH₂CH₂); 2.69 (t, 2H, J = 7.7, NCH₂CH₂CH₂); 3.21-3.31 (m, 2H, CH); 3.64 (t, 2H, J = 7.3, NCH₂CH₂CH₂); 7.12-7.46 (m, 10H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) 10.4 (CH₃); 29.5 (NCH₂CH₂CH₂); 29.8 (CH₂CH₃); 33.3 (NCH₂CH₂CH₂); 38.4 (CH₂-Cq); 38.7 (NCH₂CH₂CH₂); 52.5 (CH); 64.3 (Cq); 126.2, 128.5, 128.6, 129.1, 129.7, 130.9 (CH_{ar}); 133.1 (N-Cq_{ar}); 141.3 (CH₂-Cq_{ar});

155.3 (NC=ON); 175.9 (Cq-C=O). IR (cm⁻¹) 2958; 2914; 1704; 1450; 1416; 741; 695; 645. mp. 118-120 °C

(2R,6S)/(2RS,6RS)-1-Benzyl-2,6-diethyl-4-piperidone (42b): C₁₆H₂₃NO (245.4 g/mol), yield: 91 % (oil); *cis-trans*-ratio: 2:1 ¹H NMR (CDCl₃, δ = ppm, J = Hz) *cis*-isomer: 0.97 (t, 6H, J = 7.5, CH₂CH₃); 1.36-1.66 (m, 4H, CH₂CH₃); 2.09 (dd, 2H, ²J = 13.9, ³J_{aa} = 11.9, CH₂C=O); 2.40 (dd, 2H, ²J = 13.9, ³J_{ae} = 1.8, CH₂C=O); 2.72-2.82 (m, 2H, CHCH₂CH₃); 3.08 (s, 2H, NCH₂); 7.24-7.50 (m, 5H, CH_{ar}), *trans*-isomer: 0.94 (t, 6H, J = 7.3, CH₂CH₃); 1.36-1.66 (m, 4H, CH₂CH₃); 2.20 (ddd, 2H, ³J_{ae} = 1.4, ³J_{aa} = 6.7, ²J = 13.9, CH₂C=O); 2.49 (ddd, 2H, ³J_{ae} = 1.4, ³J_{ee} = 4.7, ²J = 13.9, CH₂C=O); 3.02-3.13 (m, 2H CHCH₂CH₃); 3.64, 4.02 (2d, 2H, J = 13.9, NCH₂); 7.24-7.50 (m, 5H, CH_{ar}). ¹³C NMR (CDCl₃, δ = ppm) *cis*-isomer: 10.0 (CH₃); 29.6 (CH₂CH₃); 47.9 (CH₂); 57.9 (CH₂); 64.6 (CHCH₂CH₃); 126.8, 128.2, 128.3, 129.1, 130.5, 133.3 (CH_{ar} *cis* and *trans*); 139.9 (Cq_{ar}); 209.7 (C=O), *trans*-isomer: 10.7 (CH₃); 25.7 (CH₂CH₃); 42.6 (CH₂); 57.5 (CH₂); 63.2 (CHCH₂CH₃); 126.8, 128.2, 128.3, 129.1, 130.5, 133.3 (CH_{ar} *trans* and *cis*); 141.4 (Cq_{ar}); 210.2 (C=O). IR (cm⁻¹) 3028; 2963; 2874; 2801; 1707; 1453; 731; 698.

1-Benzyl-4-phenylamino-piperidine-4-carbonitrile (43a): C₁₉H₂₁N₃ (291.4 g/mol), yield: 62 %, mp. 146-148 °C.

(2R,6S)-1-Benzyl-2,6-diethyl-4-phenylamino-piperidine-4-carbonitrile (43b): C₂₃H₂₉N₃ (347.5 g/mol), yield: 59 %; ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) 0.79 (CH₃); 1.26-1.39 (m, 2H, CH₂CH₃); 1.48-1.60 (m, 4H, CH₂CH₃, CqCH₂ axial); 2.31 (d, 2H, ²J = 13.4, CqCH₂ äquatorial); 2.70-2.80 (CH); 3.70 (s, 2H, NCH₂); 6.04 (s, 1H, NH); 6.75 (t, 1H, J = 7.3, CH_{ar}); 6.88 (d, 2H, J = 7.8, CH_{ar}); 7.14-7.23 (m, 4H, CH_{ar}); 7.28 (t, 2H, J = 7.6, CH_{ar}); 7.38 (d, 2H, J = 7.6, CH_{ar}). ¹³C-NMR (DMSO-d₆, δ = ppm) 10.4 (CH₃); 26.5 (CH₂CH₃); 37.3 (CqCH₂); 50.2 (NCH₂); 53.2 (Cq); 60.8 (NCH); 121.1 (CN); 125.8, 118.5, 126.0, 127.2, 127.9, 129.0 (CH_{ar}); 142.3, 144.7 (Cq_{ar}). IR (cm⁻¹) 3375; 2966; 2934; 2877; 2229; 1601; 1499; 1317; 759; 730; 696. mp. 123-125 °C.

(2R,6S)-8-Benzyl-7,9-diethyl-3-(4-nitro-benzyl)-1-phenyl-1,3,8-triaza-spiro[4.5]decane-2,4-dione (45): C₃₁H₃₄N₄O₄ (526.6 g/mol), yield: 46 %; ¹H NMR (CDCl₃, δ = ppm, J = Hz) 0.76 (t, 6H, J = 7.3, CH₂CH₃); 1.04-1.17 (m, 2H, CH₂CH₃); 1.56-1.73 (m, 6H, CH₂CH₃, CH₂-Cq); 3.29-3.40 (m, 2H, CH); 3.44 (s, 2H, CHNCH₂

Benzyl); 4.81 (s, 2H, O=CNCH₂ 4-Nitrobenzyl); 7.10-7.15 (m, 1H, **H4**_{Anilin}); 7.17-7.53 (m, 9H, **H2/3/5/6**_{Anilin}, **CH**_{Benzyl}); 7.56-7.62 (m, 2H, **H2/6** 4-Nitrobenzyl); 8.17-8.22 (m, 2H, **H3/5** 4-Nitrobenzyl). ¹³C NMR (CDCl₃, δ = ppm) 11.0 (CH₃); 27.8 (CH₂CH₃); 32.9 (CH₂-Cq); 41.7 (O=CNCH₂); 48.9 (CHNCH₂); 59.6 (CH); 64.7 (Cq); 124.1, 126.2; 127.3, 128.0, 129.3; 129.6, 129.9, 130.6 (CH_{ar}); 132.9 (N-Cq_{Anilin}); 142.8 (CH₂-Cq_{ar}); 143.4 (Cq_{ar}); 147.8 (Cq-NO₂); 154.7 (N-C=ON); 175.2 (Cq-C=O). IR (cm⁻¹) 2987; 2932; 2866; 1703; 1520; 1432; 1341; 742; 700. mp. 185-187 °C

8-Benzyl-1-phenyl-1,3,8-triaza-spiro[4.5]decane-4-one (47):

C₂₀H₂₃N₃O (321.4 g/mol), yield: 68 %; ¹H NMR (DMSO-d₆, δ = ppm, J = Hz) 1.57 (d, 2H, J = 13.6, CqCH₂); 2.52-2.63 (m, 2H, CqCH₂); 2.67-2.78 (m, 4H, NCH₂CH₂); 3.52 (s, 2H, NCH₂ Benzyl); 4.57 (s, 2H, NCH₂N); 6.76 (t, 2H, J = 7.8, CH_{ar}); 6.87 (d, 1H, J = 7.1, CH_{ar}); 7.21-7.39 (m, 7H, CH_{ar}); 8.60 (s, 1H, NH). ¹³C NMR (DMSO-d₆, δ = ppm) 28.4 (CqCH₂); 49.2 (NCH₂CH₂); 58.2 (NCH₂N); 58.7 (NCH₂ Benzyl); 62.1 (Cq); 114.3, 117.7, 126.8, 128.2, 128.7, 129.0 (CH_{ar}); 138.7, 143.3 (Cq_{ar}); 176.2 (C=ONH). IR (cm⁻¹) 3180; 3108; 3067; 2960; 2926; 2818; 1703; 1599; 1373; 1312; 1098; 1030; 796; 735; 689. mp. 234-237 °C.

1-(3-Phenylpropyl)-4-piperidine oxime (48):

Yield: 13.84 (59%). C₁₄H₂₀N₂O (232.3 g/mol); ¹H NMR (d₄-MeOH, δ = ppm, J = Hz): 7.14 – 7.18 (5 H, m, Ph-H), 3.21 – 3.14 (4 H, m, Ph-CH₂-CH₂-CH₂-N), 2.99 (2 H, t, J = 4.6, 2-H_{eq}, 6-H_{eq}), 2.77 - 2.64 (2 H, m, 2-H_{ax}, 6-H_{ax}), 2.60 - 2.49 (4 H, m, 3-H, 5-H), 2.03 – 1.95 (2 H, m, Ph-CH₂-CH₂-CH₂-N). ¹³C NMR (d₄-MeOH, δ = ppm): 151.3 (–C=N), 141.6 (C-1 arom.), 129.7, 129.5 (C-2, C-2, C-2, C-6 arom.), 127.5 (C-4 arom.), 57.6 (Ph-CH₂-CH₂-CH₂-N), 53.7 and 52.5 (C-2, C-6, rotameres), 33.7 (Ph-CH₂-CH₂-CH₂-N), 29.3 (Ph-CH₂-CH₂-CH₂-N), 27.4 and 22.5 (C-3, C-5, rotameres), IR (ATR, cm⁻¹): 3147 (OH), 3074 (=C–H), 2946 (–CH₂), 1656 (–C=N), 1600 (–C=C- arom.), 954 (N–O), 763, 704 (out of plane). mp. 182.5 °C.

1-(2-Phenylpropyl)-4-oxo-piperidine O-(2,6-dichloro-benzyl)-oxime (49):

Yield: 0.68 g (28%). $C_{21}H_{24}N_2OCl_2$ (391.3 g/mol); 1H NMR ($CDCl_3$, δ = ppm): 7.13 – 7.04 (8 H, m, aromatic); 5.23 (2 H, s, O-CH₂), 2.58 – 2.42 (8 H, m, 2-H, 3-H, 5-H, 6-H); 2.41 – 2.31 (4 H, m, Ph-CH₂-CH₂-CH₂-N); 1.82 – 1.77 (2 H, m, Ph-CH₂-CH₂-CH₂-N). ^{13}C NMR ($CDCl_3$, δ = ppm): 152.1 (–C=N), 136.1 (C-1''), 133.4 (C-1'), 130.2 (C-2'', C-6''), 128.5, 128.4, 128.2 (C-2', C-3' C-5', C-6', C-3'', C-5''), 125.8, 125.6 (C-4', C-4''), 57.5 (CH₂-O), 53.4 (Ph-CH₂-CH₂-CH₂-N), 52.4 (Ph-CH₂-CH₂-CH₂-N), 40.7 (C-2, C-6), 33.6 (C-3, C-5), 31.1 (Ph-CH₂-CH₂-CH₂-N). IR (ATR, cm⁻¹): 3026 (=C–H); 2945 and 2812 (–CH₂), 1660 (–C=N), 1563 (–C=C- arom.), 739, 705, 700, 642 (out of plane). mp. 147 °C.

4-(1,3-Dioxolan-2-yl)-N-(3-phenylpropyl)pyridinium bromide (50):

Yield: 1.78 g (37 %) colorless crystals. $C_{17}H_{20}NO_2Br$ (350.3 g/mol); 1H NMR ($CDCl_3$, δ = ppm): 9.45 (2 H, br, 2-H, 6-H pyridine), 7.94 (2 H, br, 3-H, 5-H pyridine), 7.21 – 7.06 (m, 5 H, Ph-H), 5.88 (s, 1H, O–CH–O), 5.01 (br, 2 H, Ph-CH₂-CH₂-CH₂-N), 4.04 – 3.94 (m, 4 H, O–(CH₂)₂–O), 2.74 (t, 2 H, J = 6.6, Ph-CH₂-CH₂-CH₂-N), 2.36 – 2.29 (m, 2 H, Ph-CH₂-CH₂-CH₂-N⁺), ^{13}C NMR ($CDCl_3$, δ = ppm): 156.8 (pyridine C-4), 145.5 (pyridine C-2, C-6), 139.5 (phenyl C-1), 128.7 und 128.4 (phenyl C-2, C-3, C-5, C-6), 126.5 (pyridine C-3, C-5), 125.5 (phenyl C-4), 100.0 (O–CH–O), 65.9 (O–(CH₂)₂–O), 61.4 (Ph-CH₂-CH₂-CH₂-N), 33.1 (Ph-CH₂-CH₂-CH₂-N), 32.2 (Ph-CH₂-CH₂-CH₂-N). IR (ATR, cm⁻¹): 3026 (=C–H); 2976 and 2897 (–CH); 1708 (–C=C- aromatic); 1096 (C–O), mp. 78.1 °C.

(1,3-Dioxolane-2-yl)-N-(3-phenylpropyl)piperidine hydrobromide (51)

Yield 1.84 g (98%). $C_{17}H_{26}O_2N_1Br$ (355.1 g/mol); 1H NMR ($CDCl_3$, δ = ppm, J = Hz): 11.29 (1 H, br, NH⁺), 7.30 – 7.16 (5 H, m, arom.), 4.79 and 4.64 (1 H, d, rotameres, J = 5.6, O-CH-O), 4.08 – 3.99 (4 H, m, O-CH₂-CH₂-O), 3.70 – 3.60 (2 H, m, Ph-CH₂-CH₂-CH₂-N), 3.07 – 2.71 (4 H, m, 2-H, 6-H), 2.68 – 2.16 (7 H, m, 3-H, 4-H, 5-H, Ph-CH₂-CH₂-CH₂-N), 1.76 – 1.69 (2 H, m, Ph-CH₂-CH₂-CH₂-N). ^{13}C NMR ($CDCl_3$, δ = ppm): 139.4 (phenyl C-1), 128.8, 128.4 (phenyl C-2, C-3, C-5, C-6), 126.7 (phenyl C-4), 105.3 (O–CH–O), 66.0 (O–(CH₂)₂–O), 57.3 (Ph-CH₂-CH₂-CH₂-N), 52.6 (C-2, C-6), 38.7 (C-4),

32.9 (Ph-CH₂-CH₂-CH₂-N), 24.9 (Ph-CH₂-CH₂-CH₂-N), 23.9 (C-3, C-5). **IR** (ATR, cm⁻¹): 3029 (=C-H), 2926 and 2885 (-CH₂), 1600 (-C=C- arom.), 1045 cm⁻¹ (C-O). mp. 132 °C (dec.)

1-1-(3-Phenyl-propyl)-piperidine-4-carbaldehyde oxime (52)

Yield: 1.90 g (55 %), C₁₅H₂₂N₂O (246.4 g/mol); **¹H NMR** (CDCl₃, δ = ppm, J = Hz):

9.11 (1 H, br, OH), 7.64 – 7.10 (6 H, m, 5 H arom., HC=N), 2.91 – 2.88 (2 H, m, 2-H_{eq}, 6-H_{eq}), 2.55 (2 H, t, J = 7.8, Ph-CH₂-CH₂-CH₂-N), 2.34 – 2.30 (2 H, m, 2-H_{ax}, 6-H_{ax}), 2.14 – 1.53 (9 H, m, 3-H, 4-H, 5-H, Ph-CH₂-CH₂-CH₂-N). **¹³C NMR** (CDCl₃, δ = ppm): 154.1 (HC=N), 141.9 (C-1, arom.), 128.4, 128.3 (C-2, C-3, C-5, C-6 arom.), 125.6 (C-4 arom.), 58.3 (C-2, C-6), 53.0, Ph-CH₂-CH₂-CH₂-N, 33.7 (C-4), 29.0 (C-3, C-5), 28.4, 28.2 (Ph-CH₂-CH₂-CH₂-N). **IR** (ATR, cm⁻¹): 3050 – 2750 (OH, br), 3021 (=CH), 2937, 2827 (-CH), 1652 (C=N), 1601, 1495 (C=C, arom.), 942 (N-O), 740 and 700 cm⁻¹ (out of plane), mp. 111 °C.

4-[(2,6-Dichloro-benzyloxyimino)-methyl]-1-(3-phenyl-propyl)-piperidinium hydrochloride (53)

Yield: 0.51 g (40 %). C₂₂H₂₇Cl₃N₂O (412.5 g/mol); **¹H NMR** (d₆-DMSO, δ ppm, J = Hz): 10.28 (1 H, br, NH⁺), 7.50 – 7.18 (9 H, HC=N, 8 H arom.), 5.23 (2 H, s, CH₂-O), 3.58 – 3.38 (2 H, m, 2-H_{eq}, 6-H_{eq}), 3.00 – 2.80 (4 H, m, Ph-CH₂-CH₂-CH₂-N, 2-H_{ax}, 6-H_{ax}), 2.61 (2 H, t, J = 7.6, Ph-CH₂-CH₂-CH₂-N), 2.41 – 2.37 (1 H, m, 4-H), 2.00 – 1.68 (6 H, m, 3-H, 5-H, Ph-CH₂-CH₂-CH₂-N). **¹³C NMR** (d₆-DMSO, δ = ppm): 153.0 (C=N), 140.5 (C-1'), 136.1 (C-2'', C-6''), 132.0 (C-1''), 131.2 (C-4''), 128.6, 128.4, 128.2 (C-2', C-3', C-5', C-6', C-3'', C-5''), 126.1 (C-4'), 69.4 (CH₂-O), 55.6 (Ph-CH₂-CH₂-CH₂-N), 50.9 (C-2, C-6), 33.8 (C-4), 32.0 (Ph-CH₂-CH₂-CH₂-N), 26.0 (C-3, C-5), 24.8 (Ph-CH₂-CH₂-CH₂-N⁺). **IR** (ATR, cm⁻¹): 2910 (-CH), 2512 (NH⁺), 1715 (C=N), 1599 and 1563 (C=C, arom.), 1021 (C-O), 931 (N-O), 777, 767, 753 and 698 cm⁻¹ (out of plane), Mp.: 198 °C (dec).

Analytical Data
Entry

		C Calc found	H Calc found	N Calc found
3	C ₁₉ H ₁₉ N ₃ O ₅ (369.4 g/mol)	61.8 61.6	5.18 5.22	11.4 11.3
4	C ₂₀ H ₂₁ N ₃ O ₅ (369.4 g/mol)	62.6 62.7	5.08 5.02	7.3 7.4
5	C ₂₃ H ₂₇ N ₃ O ₇ (457.5 g/mol)	60.4 60.6	5.95 6.12	9.2 9.0
6	C ₂₃ H ₂₅ N ₃ O ₇ (455.5 g/mol)	60.7 60.5	5.53 5.74	9.2 9.5
7	C ₂₃ H ₂₅ N ₃ O ₇ (455.5 g/mol)	60.7 60.9	5.53 5.27	9.2 9.0
8	C ₂₅ H ₂₄ N ₄ O ₅ (460.5 g/mol)	65.2 65.5	5.25 5.07	12.2 12.1
9	C ₂₆ H ₂₅ N ₃ O ₅ (459.5 g/mol)	68.0 67.8	5.48 5.19	9.1 9.4
10	C ₂₄ H ₂₃ N ₃ O ₉ (497.5 g/mol)	58.0 57.8	4.66 4.89	8.5 8.3
11	C ₂₆ H ₂₇ N ₃ O ₉ , 525.5 g/mol	59.4 59.7	5.18 5.09	8.0 7.8
12	C ₂₈ H ₂₅ N ₃ O ₉ (547.6 g/mol)	61.4 61.1	4.60 4.33	7.7 7.5
13	C ₃₀ H ₂₉ N ₃ O ₉ (575.7 g/mol)	62.6 62.8	5.08 5.29	7.3 7.6
14	C ₂₈ H ₂₄ N ₃ O ₉ Cl (582.0 g/mol)	57.8 57.6	4.16 3.98	7.2 7.4
15	C ₂₉ H ₂₇ N ₃ O ₁₀ (577.5 g/mol)	60.3 60.1	4.71 4.98	7.3 7.1
16	C ₂₉ H ₂₇ N ₃ O ₉ (561.6 g/mol)	62.0 61.8	4.85 4.99	7.5 7.7
17	C ₂₈ H ₂₅ N ₃ O ₉ (547.5 g/mol)	61.4 61.7	4.60 4.58	7.7 7.6
18	C ₂₄ H ₂₅ NO ₅ (407.5 g/mol)	70.8 70.9	6.18 6.34	3.4 3.5
33	C ₁₅ H ₁₉ N ₃ O ₂ (273.3 g/mol)	65.9 65.7	7.01 6.98	15.4 15.6
34	C ₁₈ H ₂₅ N ₃ O ₂ (315.4 g/mol)	68.5 68.3	7.99 7.69	13.3 13.6
35	C ₁₉ H ₂₇ N ₃ O ₂ (329.5 g/mol)	69.3 69.1	8.26 8.46	12.8 12.6
36	C ₂₁ H ₃₁ N ₃ O ₂ (357.5 g/mol)	70.6 70.4	8.74 8.58	11.8 11.6
37	C ₁₈ H ₂₅ N ₃ O ₃ (331.4 g/mol)	65.2 65.4	7.60 7.44	12.7 12.5

38	$C_{24}H_{29}N_3O_2$	73.6	7.47	10.7
	(391.5 g/mol),	73.7	7.66	10.5
39	$C_{23}H_{26}N_4O_4$	65.4	6.20	13.3
	(422.5 g/mol)	65.6	6.04	13.1
40	$C_{25}H_{31}N_3O_2$	74.0	7.70	10.4
	(405.5 g/mol)	73.8	7.54	10.7
41	$C_{26}H_{33}N_3O_2$	74.4	7.93	10.0
	(419.6 g/mol)	74.2	7.99	9.9
44	$C_{24}H_{29}N_3O_2$	73.6	7.47	10.7
	(391.5 g/mol)	73.4	7.74	10.6
45	$C_{31}H_{34}N_4O_4$	70.7	6.51	10.6
	(526.6 g/mol)	70.5	6.69	10.7
47	$C_{20}H_{23}N_3O$	74.7	7.21	13.1
	(321.4 g/mol)	74.4	7.45	13.0
48	$C_{14}H_{20}N_2O$	72.4	8.68	12.1
	(232.3 g/mol))	72.2	8.96	12.0
49	$C_{21}H_{24}N_2OCl_2$	64.5	6.18	7.2
	(391.3 g/mol)	64.7	6.01	7.3
52	$C_{15}H_{22}N_2O$	73.1	9.00	11.4
	(246.4 g/mol)	72.9	8.88	11.7
53	$C_{22}H_{27}Cl_3N_2O$	59.8	6.16	6.3
	(412.5 g/mol)	59.9	6.27	6.5