Supporting Information

The synthetic procedures for the preparation of **2e** and D–B–A compounds **D[3π3π3π3]A**, **D[7π3]A**, **D[11]A** and **D[3π7]A** and Figures 1S, 2S and 3S.

Synthesis of 3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylic acid (2e)

Tetraethyl pentane-1,3,3,5-tetracarboxylate (2a). To a stirred solution of sodium ethanolate (171 g, 2.51 mol) and diethyl malonate (400.5 g, 2.50 mol) in 1700 mL of dry EtOH was added dropwise over 40 min ethyl acrylate (525.8 g, 5.25 mol) while keeping the temperature at 15–20 °C by means of an ice-salt bath. After stirring for another 30 min at 20 °C the reaction mixture was poured into a stirred 1M HCl solution (6 L). The ester layer was separated and the water layer extracted with ether (1600 mL and 800 mL). The combined organic layers were dried on $MgSO_4$ and filtered. Evaporation of the solvent under reduced pressure afforded crude **2a** (96%, 868.7 g) as a colourless oil. It was used in the next step without purification. ^{1}H NMR δ 1.25 (t, $J = 7.1$ Hz, 6H), 1.26 (t, $J = 7.1$ Hz, 6H), 2.17–2.23 (m, 4H), 2.29–2.35 (m, 4H), 4.13 (q, $J = 7.1$ Hz, 4H), 4.20 (q, $J = 7.1$ Hz, 4H). ^{13}C NMR δ 13.8, 14.0, 27.9, 29.3, 56.0, 60.4, 61.3, 170.5, 172.4. FT-IR $\tilde{\nu}_{max}$ 2983, 2939, 2908, 2876, 1736 (s, C=O), 1301, 1229, 1085, 1097, 1025 (lit.[1] $\tilde{\nu}_{max}$ (C=O) 1735 cm^{-1}).

Triethyl 4-oxocyclohexane-1,1,3-tricarboxylate (2b). Sodium ethanolate (333.5 g, 4.901 mol) was added to diethyl ether (1000 mL) while stirring (in this order). Tetraethyl pentane-1,3,3,5-tetracarboxylate (**2a**, 868.2 g, 2.409 mol) was added dropwise to the stirred suspension. The ether started to boil (under reflux). After completing the addition, boiling under reflux was continued for 3 h. The reaction mixture was quickly cooled to 20 °C and poured into a cold stirred 3.15 M HCl solution (1700 mL). The organic layer was separated and the water layer extracted with ether (3×200 mL). The combined organic layers were dried on $MgSO_4$ and filtered. Evaporation of the solvent under reduced pressure afforded 640.4 g (85%) of **2b** as a colourless oil. ^{1}H and ^{13}C NMR data were in accordance with those already published in refs 2 and 3, respectively. The product was used in the next step without purification.

4-Oxocyclohexanecarboxylic acid (2c). A mixture of **2b** (551.5 g, 1.754 mol) and 2 M HCl solution (3.75 L) was boiled under reflux while stirring vigorously until the ester droplets had disappeared (24 h). Then portions of 500 mL were distilled off and were replaced every time by the same volume of water. This was repeated until the temperature of the vapour was 100 °C. The remaining solution was continuously extracted with $CHCl_3$ overnight in a liquid–liquid extraction apparatus. The $CHCl_3$ extract was concentrated under reduced pressure and the remaining material was subjected to Kugelrohr distillation. The first runnings were collected at 85 °C (0.001 Torr) as a reddish oil. At 115 °C pure **2c** (192.07 g, 77%) was collected as a colourless oil which solidified upon cooling. ^{1}H NMR δ 2.00–2.13 (m, 2H), 2.20–2.31 (m, 2H), 2.33–2.44 (m, 2H), 2.47–2.56 (m, 2H), 2.78–2.87 (m, 1H), 11.41 (br s, 1H), in accordance with ref 4. ^{13}C NMR δ 28.1, 39.5, 40.3, 180.1, 210.3. FT-IR $\tilde{\nu}_{max}$ 3500–3400 (br), 2958, 2915, 2876, 2726, 2654, 2598, 1700 (br s, C=O), 1311, 1238, 948 (lit.[5] $\tilde{\nu}_{max}$ (C=O) 1730 and 1710 cm^{-1}).

2,2-Dimethylpropane-1,3-diyl di-(3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylate) (2d). A mixture of **2c** (30.77 g, 237.0 mmol), 2,2-dimethyl-1,3-propanediol (40.58 g, 389.6 mmol) and *p*-toluenesulfonic acid monohydrate (0.1 g) in toluene (300 mL) was boiled under reflux

in a Dean-Stark apparatus until the theoretical amount of water (7.8 mL) had separated (6.5 h). The reaction mixture was cooled to 20 °C and poured into a vigorously stirred 0.1 M NaOH solution (100 mL). The organic layer was separated and dried on $MgSO_4$. Filtration and evaporation of the solvent under reduced pressure afforded **2d** as a viscous and colourless oil in quantitative yield (58.53 g). ^{1}H NMR δ 0.91 (s, 6H), 0.96 (s, 12H), 1.41–1.52 (m, 4H), 1.67–1.90 (2× m, 2 × 4H), 2.17–2.22 (m, 4H), 2.34–2.42 (m, 2H), 3.28 (s, 2H), 3.47 (s, 2H), 3.51 (s, 2H), 3.93 (s, 2H). FT-IR $\tilde{\nu}_{max}$ 2955, 2869, 1731 (s, C=O), 1106, 1185.

3,3-Dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylic acid (2e). A mixture of **2d** (58.42 g) in MeOH (200 mL) and 10 M NaOH solution (53 mL) was boiled under reflux for 2h. The solvent was removed under reduced pressure and the remaining white solid was boiled under reflux with diethyl ether (265 mL) for 30 min. The suspension was filtered over a glass frit, and the residue was washed with diethyl ether (3 × 100 mL) and subsequently dissolved in water (320 mL). To the aqueous solution was added under vigorous stirring 3 M HCl solution (170 mL) and CH_2Cl_2 (320 mL). The layers were separated and to the aqueous layer was added an additional amount of 3 M HCl solution (210 mL). It was washed with CH_2Cl_2 twice (640 mL and 320 mL) immediately. The combined organic layers were dried on $MgSO_4$ and filtered. Removal of the solvent under reduced pressure afforded 42.19 g of a white solid, which was crystallized from *n*-hexane–$CHCl_3$ (4 : 1 v/v, 84.4 mg mL^{-1}; reflux to −20 °C) to yield 35.82 g (72% with respect to **2c**) of **2e** as large colourless crystals. These were stored on P_2O_5 until further use. Analytical data (^{1}H NMR and ^{13}C NMR) were in agreement with those obtained by Hoogesteger.[6,7]

Synthesis of D–B–A compounds

9-[4-Hydroxy-4'-(1-phenylpiperidin-4-ylidene)-1,1'-bi(cyclohexyliden)-4-yl]-3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylic acid (6). Coupling of ketone **5** (0.50 g, 1.49 mmol) and carboxylic acid **2e** (0.35 g, 1.54 mmol) as described for **3** gave an off-white solid (0.57 g, 68%) of mp 171 °C (dec). FT-IR $\tilde{\nu}_{max}$ 3500–3100, 3055, 3048, 2953, 2901, 2863, 2900–2300, 1713, 1680, 1493, 1447, 1103, 758, 694.

4-[4'-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-ylidene)-1,1'-bi(cyclohexyliden)-4-yli-dene]-1-phenylpiperidine (7). Decarboxylation and dehydration of β-hydroxy acid **6** (0.55 g, 0.98 mmol) using *N*,*N*-dimethylformamide dineopentyl acetal (1.01 g, 4.37 mmol) in MeCN (70 mL) as described for **4** gave **7** (0.28 g, 57%) as an off-white solid (mp 175 °C dec). ^{1}H NMR δ 0.98 (s, 6H), 1.79–1.83 (m, 4H), 2.23–2.30 (m, 20H), 2.44–2.48 (m, 4H), 3.20–3.24 (m, 4H), 3.53 (s, 4H), 6.78–6.82 (m, 1H), 6.91–6.93 (m, 2H), 7.22–7.26 (m, 2H). FT-IR $\tilde{\nu}_{max}$ 3094, 3063, 3034, 3023, 2976, 2957, 2928, 2899, 2883, 2866, 2837, 1599, 1462, 1446, 1427, 1116, 1101, 750, 683.

4''-(1-Phenylpiperidin-4-ylidene)-1,1':4',1''-ter(cyclohexan)-1(1'),1''(4')-dien-4-one (8). Hydrolysis of acetal **7** (0.28 g, 0.56 mmol) as described for **4** afforded 0.19 g (0.46 mmol, 82%) of a yellowish solid of mp 195 °C (dec). ^{1}H NMR δ 2.28–2.30 (m, 16H), 2.39–2.43 (m, 4H), 2.44–2.48 (m, 4H), 2.54–2.59 (m, 4H), 3.21–3.24 (m, 4H), 6.78–6.83 (m, 1H), 6.91–6.96 (m, 2H), 7.22–7.28 (m, 2H). ^{13}C NMR δ 26.5, 26.6, 28.8, 29.0, 29.1, 29.2, 40.5, 50.4, 115.9, 118.8, 124.1, 125.7, 128.2, 129.0, 129.1, 130.1, 132.2, 151.4, 213.0. FT-IR $\tilde{\nu}_{max}$ 3094, 3063, 3034, 3023, 2974, 2957, 2932, 2907, 2893, 2837, 2810, 1724, 1599, 1502, 1460, 1445, 1423, 750, 683.

[4''-(1-Phenylpiperidin-4-ylidene)-1,1':4',1''-ter(cyclohexan)-1(1'),1''(4')-dien-4-yli-

dene]malononitrile (D[3π3π3π3]A). Condensation of ketone **8** (0.15 g, 0.36 mmol) and malononitrile (38 mg, 0.57 mmol) as described for **D[3π3π3]A** afforded **D[3π3π3π3]A** (60 mg, 36%) as a greenish solid of mp 215 °C (dec). ^{1}H NMR δ 2.28 (s, 16H), 2.44–2.49 (m, 8H), 2.72–2.76 (m, 4H), 3.20–3.24 (m, 4H), 6.78–6.83 (m, 1H), 6.91–6.93 (m, 2H), 7.22–7.26 (m, 2H). FT-IR $\tilde{\nu}_{max}$ 3088, 3077, 3055, 2974, 2955, 2901, 2839, 2230, 1599, 1505, 1464, 1442, 1427, 750, 689. MALDI TOF-MS: m/z [M–H]$^+ = 464$.

9-[1-Hydroxy-4-(1-phenylpiperidin-4-yl)cyclohexyl]-3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylic acid (10). Compound **10** was synthesized as described for **3**, starting from carboxylic acid **2e** (4.40 g, 19.3 mmol) and ketone **9** (4.84 g, 18.8 mmol). The crude reaction mixture was poured onto ice (100 g), and after separation of the layers the aqueous layer was washed with diethyl ether (2 × 10 mL) and subsequently acidified to pH 5 (3 M HCl solution). The resulting suspension was filtered and after drying in vacuo over KOH 1.48 g (3.05 mmol) of a white solid was obtained. The organic layers were combined and concentrated in vacuo giving a brown solid which was mixed with CH_2Cl_2 (50 mL). The resulting suspension was filtered. The white residue was suspended in a mixture of acetone (60 mL) and water (30 mL). The suspension was acidified to pH 1 (3 M HCl solution) and the resulting white solid was filtered off. After drying an additional crop of **10** (3.55 g, 7.32 mmol) was obtained. Total yield: 5.03 g (54%) of mp 210 °C (dec). FT-IR $\tilde{\nu}_{max}$ 3500–3300, 3090, 2947, 2931, 2920, 2839, 1674, 1464, 767.

4-[4-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-ylidene)cyclohexyl]-1-phenylpiperidine (11). This compound was synthesized as described for **4** starting from β-hydroxy acid **10** (3.55 g, 7.32 mmol) and *N*,*N*-dimethylformamide dineopentylacetal (5.74 g, 24.8 mmol) in MeCN (600 mL). An off-white solid (2.05 g, 66%) was isolated: mp 196 °C (dec). ^{1}H NMR δ 0.98 (s, 6H) superposed on 0.95–1.05 (m, 2H), 1.15–1.25 (m, 1H), 1.30–1.49 (m, 3H), 1.67–1.88 (m, 10H), 2.18–2.35 (m, 4H), 2.59–2.67 (m, 2H), 2.72–2.76 (m, 2H), 3.53 (s, 4H), 3.68–3.72 (m, 2H), 6.79–6.84 (m, 1H), 6.93–6.96 (m, 2H), 7.22–7.27 (m, 2H). ^{13}C NMR δ 22.8, 25.1, 29.6, 30.3, 31.6, 33.7, 41.1, 42.9, 50.4, 70.1, 97.8, 113.5, 116.5, 119.2, 127.3, 129.0, 130.3, 152.0. FT-IR $\tilde{\nu}_{max}$ 3091, 3062, 2953, 2854, 1601, 1502, 1464, 1445, 750, 687.

4'-(1-Phenylpiperidin-4-yl)-1,1'-bi(cyclohexyliden)-4-one (12). Ketone **12** was obtained by hydrolysis of acetal **11** (543 mg, 1.28 mmol) as described for **5**. A white solid was obtained (429 mg) that consisted of **12** and ca. 4% 2,2-dimethyl-1,3-propanediol (^{1}H NMR). ^{1}H NMR δ 0.98–1.12 (m, 2H), 1.17–1.28 (m, 1H), 1.33–1.51 (m, 3H), 1.7–1.93 (m, 6H), 2.38–2.42 (m, 4H), 2.55–2.74 (m, 8H), 3.69–3.73 (m, 2H), 6.79–6.86 (m, 1H), 6.93–6.96 (m, 2H), 7.22–7.27 (m, 2H). ^{13}C NMR δ 26.6, 29.5, 29.6, 31.2, 40.8, 40.9, 42.6, 50.3, 116.4, 119.2, 123.3, 129.0, 133.2, 151.9, 212.7. FT-IR $\tilde{\nu}_{max}$ 3059, 2943, 2908, 2843, 1715, 1599, 1494, 1444, 761, 692.

[4'-(1-Phenylpiperidin-4-yl)-1,1'-bi(cyclohexyliden)-4-ylidene]malononitrile (D[7π3]A). Condensation of ketone **12** (428 mg, 1.27 mmol) and malononitrile (113 mg, 1.72 mmol) using ammonium acetate (105 mg, 1.36 mmol) and acetic acid (0.23 mL, 4.0 mmol) in benzene (35 mL) was conducted as described for **D[3π3π3]A**. After evaporation of ca. 25 mL benzene a greenish suspension was obtained, which was mixed with $CHCl_3$ (50 mL). The resulting solution was washed with saturated $NaHCO_3$ solution. Evaporation afforded a greenish solid which was further purified by column chromatography (eluent: $CHCl_3$–MeOH, 100 : 1 v/v). Recrystallization from MeCN–CH_2Cl_2 (10 : 1 v/v, 55 mL) afforded pure **D[7π3]A** as a white solid (260 mg, 54%) of mp 210 °C (dec). ^{1}H NMR δ 0.96–1.09 (m, 2H), 1.18–1.28 (m, 1H), 1.32–1.50 (m, 3H), 1.74–1.92

(m, 6H), 2.46–2.50 (m, 4H), 2.60–2.76 (m, 8H), 3.69–3.73 (m, 2H), 6.80–6.85 (m, 1H), 6.93–6.95 (m, 2H), 7.22–7.27 (m, 2H). ^{13}C NMR δ 28.2, 29.5, 29.7, 31.2, 34.6, 40.9, 42.6, 50.3, 82.9, 111.6, 116.5, 119.3, 122.3, 129.0, 134.4, 151.8, 184.9. FT-IR $\tilde{\nu}_{max}$ 3090, 2955, 2940, 2911, 2830, 2230, 1597, 1500, 1433, 752, 685.

4-[*cis/trans*-4-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl)cyclohexyl]-1-phenylpiperidine (13). Acetal **11** (1.49 g, 3.52 mmol) in THF (100 mL) was hydrogenated in a Parr apparatus (4 atm H_2) using 5% Pd/C as a catalyst. After 48 h the catalyst was removed by filtration over celite and the colourless filtrate was concentrated in vacuo. A white solid was obtained in quantitative yield which proved to consist of *cis* and *trans* **13** in a ratio of ca. 1 : 6 (^{1}H NMR). No attempt was made to separate the isomers. ^{1}H NMR (*trans* isomer) δ 0.96 (s, 6H) superposed on 0.91–1.88 (m, 22H), 2.23–2.27 (m, 2H), 2.59–2.68 (m, 2H), 3.46 (s, 2H), 3.72 (s, 2H), 3.68–3.72 (m, 2H), 6.80–6.84 (m, 1H), 6.93–6.95 (m, 2H), 7.22–7.26 (m, 2H).

***trans*-4'-(1-Phenylpiperidin-4-yl)-1,1'-bi(cyclohexyl)-4-one (14).** Hydrolysis of acetal **13** (mixture of isomers, 1.16 g, 2.73 mmol) as described for **5** afforded a white solid (0.80 g, 80%). The *trans* isomer was isolated by recrystallization from hot MeOH. Yield: 279 mg (30%). Mp 182 °C (dec). ^{1}H NMR δ 1.00–1.23 (m, 7H), 1.36–1.62 (m, 5H), 1.77–1.86 (m, 6H), 2.02–2.07 (m, 2H), 2.27–2.43 (m, 4H), 2.61–2.67 (m, 2H), 3.68–3.72 (m, 2H), 6.79–6.85 (m, 1H), 6.93–6.95 (m, 2H), 7.22–7.27 (m, 2H). ^{13}C NMR δ 29.3, 29.7, 30.0, 30.2, 40.9, 41.2, 41.4, 41.8, 42.4, 50.2, 116.3, 119.0, 128.8, 151.8, 212.2. FT-IR $\tilde{\nu}_{max}$ 3094, 3065, 2940, 2908, 2843, 1723, 1599, 1496, 1447, 762, 692.

[*trans*-4'-(1-Phenylpiperidin-4-yl)-1,1'-bi(cyclohexyl)-4-ylidene]malononitrile (D[11]A). Condensation of ketone **14** (279 mg, 0.82 mmol) and malononitrile (110 mg, 1.66 mmol) using ammonium acetate (86 mg) and acetic acid (0.20 mL) in benzene (70 mL) as described for **D[3π3π3]A** afforded a greenish solution. The solvent was removed until a solid started to precipitate. The suspension was cooled to −20 °C and a greenish solid was filtered off. Recrystallization from CH_2Cl_2–MeOH (1 : 1 v/v) afforded pure **D[11]A** as a white solid (176 mg, 55%) of mp 210 °C (dec). ^{1}H NMR δ 0.99–1.48 (m, 12H), 1.76–1.86 (m, 6H), 2.02–2.09 (m, 2H), 2.26–2.36 (m, 2H), 2.60–2.68 (m, 2H), 3.03–3.08 (m, 2H), 3.72 (m, 2H), 6.80–6.84 (m, 1H), 6.93–6.95 (m, 2H), 7.31–7.27 (m, 2H). ^{13}C NMR δ 29.4, 30.0, 30.2, 31.0, 34.4, 41.3, 41.9 (2×), 42.5, 50.4, 82.4, 111.7, 116.5, 119.2, 129.0, 151.9, 185.0. FT-IR $\tilde{\nu}_{max}$ 3090, 2949, 2930, 2908, 2847, 2230, 1593, 1502, 1445, 1410, 756, 686.

Neopentyl 4-oxocyclohexanecarboxylate (15). To a stirred solution of 4-oxocyclohexanecarboxylic acid (**2c**) (55.44 g, 390.0 mmol, which had been stored on P_2O_5) and pyridine (31.65 g, 400.1 mol, dried on 4 Å molecular sieves) in ether (400 mL) was added a solution of oxalyl chloride (50.82 g, 400.4 mmol) in ether (200 mL) in 30 min, while keeping the temperature between −5 and 0 °C. A white suspension formed and the evolution of gas was visible. Subsequently, the mixture was stirred for 24 h at room temperature. Then it was cooled to −5 °C and a solution of 2,2-dimethylpropan-1-ol (36.13 g, 409.9 mmol) and pyridine (33.96 g, 429.3 mmol) in ether was added in 35 min, while keeping the temperature below 0 °C. The mixture was stirred for 24 h and subsequently filtered over a glass fritt. The residue was extracted with ether (3 × 150 mL). The combined filtrates were washed with a 0.1 M HCl solution (2 × 50 mL) and water (50 mL) and dried on $MgSO_4$. Filtration and removal of the solvent under reduced pressure afforded a clear yellowish oil, which was subjected to vacuum distillation using a Vigreux column of 10 cm. At 92–104 °C (0.005 mm Hg) 55.69 g (67%) of pure **15** was collected as a colourless oil. ^{1}H NMR δ 0.96 (s, 9H), 1.98–2.11 (m, 2H), 2.19–2.28

(m, 2H), 2.31–2.42 (m, 2H), 2.44–2.53 (m, 2H), 2.80 (tt-like, $J = 4.0$ Hz and $J = 9.6$ Hz, 1H), 3.82 (s, 2H). ^{13}C NMR δ 26.4, 28.5, 31.3, 39.7, 40.8, 73.9, 174.0, 209.8. FT-IR $\tilde{\nu}_{max}$ 2958, 2908, 2872, 1720, 1380, 1366, 1214–1178, 1031, 1008, 752.

Neopentyl 4-(3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-9-ylidene)cyclohexanecarboxylate (16a). To a stirred solution of *N*,*N*-diisopropylamine (20.44 g, 202.0 mmol) in THF (160 mL), cooled to −40 °C was added 1.59 M *n*-butyllithium in hexanes (128 mL, 204 mmol). The mixture was allowed to warm to −15 °C in 35 min. Subsequently, it was cooled to −40 °C and **2e** (22.83 g, 100.0 mmol) was added as a solid. The temperature was allowed to rise to −30 °C and the mixture was gently heated to 50 °C at which temperature butane evolved. After 1 h at 50 °C the reaction mixture was cooled again to −40 °C. A solution of **15** (21.60 g, 101.7 mmol) in THF (30 mL) was added in 5 min while maintaining the temperature at −40 °C. At this temperature, the clear and slightly yellow reaction mixture was stirred for another 30 min. Then it was stirred for 1 h at 50 °C and overnight at 20 °C. The reaction mixture was poured into a mixture of 2M HCl (220 mL) and ice (220 g) and subsequently extracted with $CHCl_3$ (400 mL and 2 × 200 mL). The combined organic layers were dried with $MgSO_4$. Filtration and removal of the solvent under reduced pressure afforded an off-white solid. The solid was extracted with *n*-pentane in a Soxhlett apparatus overnight. The extract (9.25 g after removal of solvent) consisted of a mixture of unreacted **2e** and **15**. According to NMR the white residue (31.12 g) did not contain any starting material.

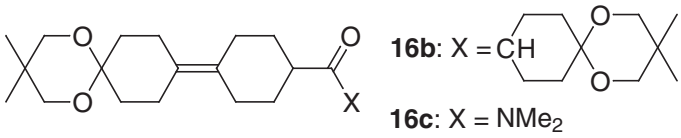

Chart 1:

The residue (31.12 g) was stirred in MeCN (440 mL) and *N*,*N*-dimethylformamide dineopentylacetal (32.76 g, 141.6 mmol) was added. After stirring for 1 h at 20 °C all solid had disappeared and the reaction mixture was heated at reflux temperature overnight. To the cooled mixture was added toluene (1 L) upon which it was washed with a mixture of water (600 mL) and saturated NH_4Cl solution (100 mL). The organic layer was dried on $MgSO_4$. Filtration and removal of the solvent under reduced pressure yielded 31.92 g of a beige solid. Column chromatography (eluent *n*-pentane–ethyl acetate, 10 : 1 v/v, gradually changed to 0 : 1) afforded pure **16a** (14.79 g, 39% relative to **2e**) as a white solid. Two other compounds were isolated (Chart 1): 3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl[4-(3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-9-ylidene)cyclohexyl]methanone (**16b**, 2.98 g, 12% relative to **2e**) and 4-(3,3-dimethyl-1,5-dioxaspiro[5.5]decan-9-ylidene)-*N*,*N*-dimethylcyclohexanecarboxamide (**16c**, 3.36 g, 10% relative to **2e**). Analytical samples were prepared by crystallization from MeOH (**16a**: 43 mg mL^{-1}; **16b**: 5.1 mg mL^{-1}; **16c**: 92 mg mL^{-1}) yielding colourless crystals for all compounds. Analytical data of **16a**: mp 128–129 °C. TLC (*n*-pentane–ethyl acetate, 5 : 1 v/v) $R_f = 0.49$. ^{1}H NMR δ 0.94 (s, 9H), 0.98 (s, 6H), 1.44–1.57 (m, 2H), 1.73–1.88 (m, 6H), 1.96–2.04 (m, 2H), 2.17–2.32 (m, 4H), 2.52 (tt-like, J = 4.0 Hz and J = 11.0 Hz, 1H), 2.65–2.72 (m, 2H), 3.52 (s, 4H), 3.76 (m, 2H). ^{13}C NMR (APT) δ 43.5 (CH); 22.7, 26.4 (CH_3); 30.2, 31.4, 97.7, 128.4, 128.5, 175.6 (q); 25.1, 28.5, 30.4, 33.5, 70.1, 73.4 (CH_2). FT-IR $\tilde{\nu}_{max}$ 2979–2937, 2907, 2865, 2845, 1728 (s, C=O), 1137, 1217, 1169, 1122–1105, 920, 909, 899, 864, 636. Analytical data of **16b**: mp 186–

191 °C. TLC (*n*-pentane–ethyl acetate, 5 : 1 v/v) $R_f = 0.23$. ^{1}H NMR δ 0.96 (s, 6H), 0.97 (s, 6H), 1.31–1.44 (m, 4H), 1.57–1.88 (m, 12H), 2.15–2.31 (m, 6H), 2.52 (tt-like, J = 4.2 Hz and J = 10.7 Hz, 1H), 2.69 (tt-like signal, 1H) superposed on 2.69–2.77 (m, 2H), 3.45 (s, 2H), 3.51 (s, 6H). ^{13}C NMR (APT) δ 48.3, 49.2 (CH); 2 × 22.7 (resolved, 2 × CH_3); 30.1, 30.2, 96.8, 97.6, 128.3, 128.5, 215.6 (q); 24.5, 25.0, 28.7, 30.0, 31.4, 33.5, 69.8, 70.0 (CH_2). FT-IR $\tilde{\nu}_{max}$ 2949, 2939, 2863, 1708 (s, C=O), 1129, 1111, 1099, 921, 911, 898, 860. Analytical data of **16c**: mp 154–156 °C. TLC (ethyl acetate) $R_f = 0.30$. ^{1}H NMR δ 0.97 (s, 6H), 1.45–1.59 (m, 2H), 1.71–1.88 (m, 8H), 2.15–2.33 (m, 4H), 2.69 (tt-like, J = 3.6 Hz, J = 11.4 Hz, 1H), 2.77–2.83 (m, 2H), 2.93 (s, 3H), 3.07 (s, 3H), 3.52 (s, 4H). ^{13}C NMR (APT) δ 40.9 (CH); 22.7, 35.5, 37.1 (CH_3); 30.2, 97.7, 128.3, 128.4, 175.5 (q); 25.0, 28.8, 30.4, 33.4, 70.0, 70.1 (CH_2). FT-IR $\tilde{\nu}_{max}$ 2974, 2953–2918, 2864, 2840; 1648, 1640 (s, C=O); 1129–1099, 919, 909, 897, 868.

Neopentyl *cis/trans*-4-(3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl)cyclohexanecarboxylate (17). A solution of **16a** (13.64 g, 36.03 mmol) in a mixture of THF (400 mL) and EtOH (100 mL) was stirred under 1 atm. of H_2 for 3 days in the presence of a catalytic amount of 10% Pd/C. After that period GC analysis showed that no starting compound was present anymore; two peaks of equal intensity were visible, presumably corresponding to the *cis* and *trans* isomer of the product. The catalyst was removed by filtration over celite. Evaporation of the solvent under reduced pressure afforded **17** (13.43 g, 98%) as a white solid. ^{1}H NMR gave a signal for the axial proton next to the carboxyl group in the *cis* isomer at 2.55–2.61. The product was used in the next step without separation and full spectral analysis of the isomers.

***cis/trans*-4-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl)cyclohexanecarboxylic acid (18).** A solution of **17** (7.51 g, 19.7 mmol) in MeOH (110 mL) and 10 M aqueous NaOH solution (5.3 mL, 53 mmol) was heated at reflux temperature for 12 h. The solvent was removed under reduced pressure and the remaining solid was extracted overnight with *n*-pentane in a Soxhlett apparatus. The remaining solid was dissolved in water (400 mL) and three portions of 10 mL of a 3 M HCl solution were added. After the addition of each portion the mixture was immediately extracted with CH_2Cl_2 (150 mL) and finally with another 100 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure afforded **18** (4.48 g, 73%) as a mixture of the *cis* and *trans* isomers. A crystallization from *n*-hexane–$CHCl_3$ (10 : 2 v/v; 37 mg mL^{-1}) yielded pure *trans* isomer as colourless crystals, mp 175–179 °C, for which the following analytical data were obtained: ^{1}H NMR δ 0.96 (s, 6H) superimposed on 0.95–1.46 (m, 10H), 1.57–1.60 (m, 2H), 1.79–1.83 (m, 2H), 2.00–2.05 (m, 2H), 2.22 (tt-like signal, 1H) superposed on 2.22–2.27 (m, 2H), 3.46 (s, 2H), 3.52 (s, 2H). ^{13}C NMR (APT) δ 41.6, 42.4, 43.2 (CH); 22.7 (CH_3); 30.2, 97.8, 182.1 (q); 25.7, 29.0, 29.2, 32.2, 69.8, 70.0 (CH_2). FT-IR $\tilde{\nu}_{max}$ 3500–2500, 2975, 2947, 2923, 2861, 2723, 2668, 2620, 2564, 2534, 1691 (s, C=O), 1110, 1101, 526, 504.

4-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl)-1-(4-hydroxy-1-phenylpiperidin-4-yl)cyclohexanecarboxylic acid (20). To a cooled (−70 °C) solution of diisopropylamine (0.76 g, 7.51 mmol) in THF (15 mL) was added 2.5 M *n*-butyllithium in hexanes (2.63 mL, 6.58 mmol). The solution was warmed up to 0 °C and then recooled to −40 °C after which **18** (*cis*/*trans* mixture, 0.97 g, 3.12 mmol) and TMEDA (0.99 mL, 6.56 mmol) were added. The mixture was gently heated to 50 °C and was kept at that temperature for 1 h. Thereafter it was recooled to −70 °C. A solution of 1-phenylpiperidin-4-one (**19**)[8] (0.55 g, 3.14 mmol) in THF (5 mL) was added. The mixture was gently warmed to 50 °C, kept at that temperature for 1 h and stirred overnight at room temperature.

The reaction mixture was poured into ice (400 g) and extracted with *n*-pentane (3×200 mL). The water layer was carefully acidified with HCl (1 M) to pH 3–4. The precipitate formed was filtered off and dried under reduced pressure yielding **20** (1.00 g, 66%) as an off-white solid, mp 221 °C (dec). FT-IR $\tilde{\nu}_{max}$ 3500–2500, 3413, 2947, 2860, ∼1900 (w, br), 1691 (s, C=O), 1599, 1495, 1464, 1447, 1110, 768, 699.

4-[4-(3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl)cyclohexylidene]-1-phenylpiperidine (21). To a stirred suspension of **20** (1.00 g, 2.06 mmol) in MeCN (50 mL) was added *N*,*N*-dimethylformamide dineopentyl acetal (1.00 g, 4.32 mmol). After 1 h at room temperature the mixture was heated to reflux temperature and allowed to react overnight. The reaction mixture was cooled to −20 °C. The precipitate which formed, was filtered off and washed with cold MeCN. Drying under vacuum yielded pure **21** (227 mg, 26%) as a white solid, mp 176 °C. ^{1}H NMR δ 0.96 (s, 6H) superposed on 0.93–1.06 (m, 2H), 1.17–1.36 (m, 10H), 1.65–1.85 (m, 4H), 2.23–2.27 (m, 2H), 2.38–2.51 (m, 4H), 2.69–2.73 (m, 2H), 3.14–3.26 (m, 2H), 3.46 (s, 2H), 3.52 (s, 2H), 6.77–6.83 (m, 1H), 6.89–6.94 (m, 2H), 7.20–7.28 (m, 2H). ^{13}C NMR δ 22.7, 25.9, 29.0, 29.5, 30.2, 31.7, 32.3, 42.2, 42.8, 50.6, 69.8, 70.1, 97.8, 115.9, 118.8, 124.6, 129.0, 131.4, 151.5. FT-IR $\tilde{\nu}_{max}$ 3096, 3071, 3038, 3025, 2976, 2953, 2903, 2845, 1601, 1505, 1464, 1442, 1433, 1221, 1111, 1099, 916, 750, 687, 521, 502.

4'-(1-phenylpiperidin-4-ylidene)-1,1'-bi(cyclohexan)-4-one (22). A mixture of **21** (227 mg, 0.536 mmol) in THF (33 mL) and 5% HCl solution (3.3 mL) was heated at reflux temperature for 1 h. It was then poured into water (15 mL) and extracted with $CHCl_3$ (2×50 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (25 mL) and water (25 mL), dried on $MgSO_4$, filtered and concentrated under reduced pressure. The white solid obtained was purified by flash chromatography over silica using CH_3Cl_3–acetone (10 : 1 v/v). Removal of the solvent under reduced pressure yielded **22** (170 mg, 94%). An analytical sample was prepared by crystallization from MeOH, mp 200 °C. ^{1}H NMR δ 0.98–1.12 (m, 2H), 1.40–1.64 (m, 4H), 1.72–1.88 (m, 4H), 2.00–2.08 (m, 2H), 2.25–2.52 (m, 8H), 2.73–2.78 (m, 2H), 3.14–3.28 (m, 4H), 6.78–6.83 (m, 1H), 6.89–6.94 (m, 2H), 7.21–7.28 (m, 2H). ^{13}C NMR δ 29.0, 29.4, 29.9, 31.7, 41.1, 41.3, 42.2, 50.6, 115.9, 118.8, 125.2, 129.0, 130.8, 151.4, 212.4. FT-IR $\tilde{\nu}_{max}$ 3092, 3063, 3040, 3023, 2990, 2971, 2955, 2942, 2907, 2888, 2847, 2812, 1723 (s, C=O), 1597, 1505, 1460, 1443, 1424, 1217, 922, 754, 689, 509.

2-[4'-(1-phenylpiperidin-4-ylidene)-1,1'-bi(cyclohexan)-4-ylidene]malononitrile (D[3π7]A). A mixture of **22** (100 mg, 0.296 mmol), malononitrile (44 mg, 0.67 mmol), ammonium acetate (34 mg, 0.44 mmol) and acetic acid (0.085 mL, 1.5 mmol) in benzene (50 mL) was boiled under the removal of water in a Dean-Stark apparatus for 3 h. The solvent was evaporated under reduced pressure and the remaining solid was subjected to column chromatography (200 g silica; eluent $CHCl_3$). This yielded pure **D[3π7]A** as a white solid (71 mg, 62%), mp 209 °C. ^{1}H NMR δ 0.94–1.08 (m, 2H), 1.23–1.52 (m, 4H), 1.70–1.84 (m, 4H), 2.05–2.11 (m, 2H), 2.26–2.36 (m, 2H), 2.45 (t-like, $J = 6.2$ Hz, 4H), 2.72–2.77 (m, 2H), 3.03–3.10 (m, 2H), 3.21 (t-like, $J = 5.8$ Hz, 4H), 6.78–6.83 (m, 1H), 6.90–6.93 (m, 2H), 7.22–7.27 (m, 2H). ^{13}C NMR δ 28.97, 29.25, 31.04, 31.52, 34.33, 41.49, 42.11, 50.56, 82.48, 111.65, 115.90, 118.86, 125.40, 129.04, 130.42, 151.35, 184.84. FT-IR $\tilde{\nu}_{max}$ 3094, 3071, 3038, 3021, 2951, 2913, 2897, 2831, 2816, 2230 (s, C≡N), 1597, 1503, 1460, 1443, 1427, 1219, 912, 760, 691, 519. MALDI TOF-MS: m/z $[M–H]^+ = 386$.

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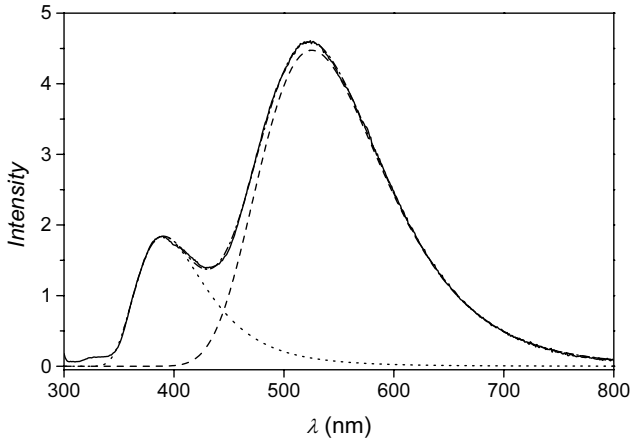

Figure 1S: Fit (dash dot, falls under solid line) to the steady state fluorescence spectrum of **D[3π3]A** in cyclohexane (solid line) as obtained by deconvolution by two skewed Gaussians (equation 3).

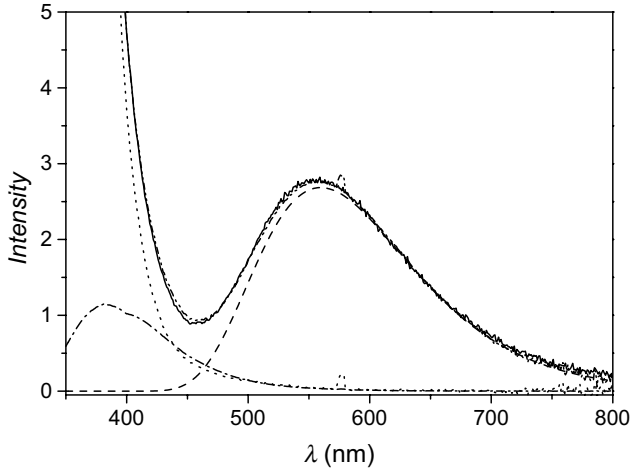

Figure 2S: Fit (dash dot dot) to the steady state fluorescence spectrum of **D[7π3]A** in di-*n*-butyl ether (solid line) as obtained by deconvolution by the experimental spectra of **D[7]** (dot) and **[3π3]A** (dash dot) in di-*n*-butyl ether and one skewed Gaussian (dash; equation 3).

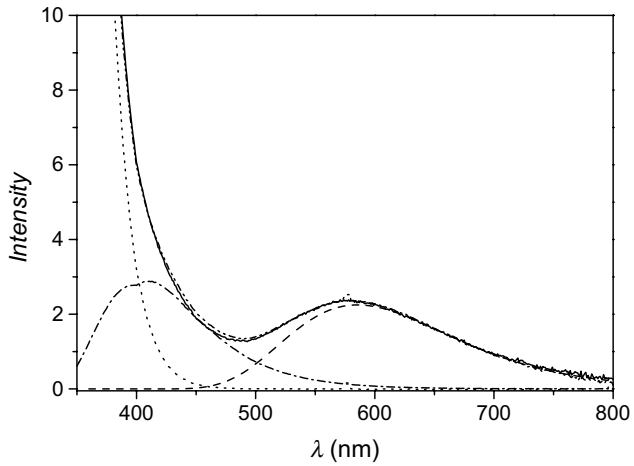

Figure 3S: Fit (dash dot dot) to the steady state fluorescence spectrum of **D[7π3]A** in diethyl ether (solid line) as obtained by deconvolution by the experimental spectra of **D[7]** (dot) and **[3π3]A** (dash dot) in diethyl ether and one skewed Gaussian (dash; equation 3).