Syntheses of chiral hosts

The \((R,R)\) TADDOL 1 and isothiocyanate 3a were previously described and their physical properties match those reported in the literature [19].

Isocyanate 3b: in a round-bottom flask a solution of TADDAMINE 2 (464 mg, 1 mmol) in dichloromethane (10 mL), was stirred with triethylamine (1.2 mL, 9 mmol); a solution of triphosgene (297 mg, 3 mmol) in dichloromethane (2 mL) was added dropwise, over five min. After one hour, water was added and the reaction mixture was extracted with diethyl ether (3×10 mL). The reunited organic layers were dried over sodium sulphate and the solvent evaporated. Purification by column chromatography (silicagel – 10% EE/PE) afforded the bis-isocyanate 3b (97%) as a colourless solid (m.p. = 191-2ºC; lit. [19] = 196-7ºC).

Synthesis of bis-(thio)ureas, general procedure GP-1: to a stirred suspension of isothiocyanate 3a or solution of isocyanate 3b (0.5 mmol) in diethyl ether (10 mL) was added the corresponding amine (1 mmol). A white precipitate was formed soon after the addition of the amine. The reaction was monitored by TLC and after 3 hours was stopped. The product was filtered, washed with diethyl ether and dried under vacuum.

Synthesis of amino-(thio)ureas, general procedure GP-2: to a suspension of TADDAMINE 2 (232 mg, 0.5 mmol) in diethyl ether (10 mL) was added the iso(thio)cyanate (0.6 mmol) and the mixture stirred at room temperature for 3 hours. A precipitate was formed during the reaction indicating the formation of the amino-(thio)urea. The reaction was monitored by TLC and after the consumption of the TADDAMINE the precipitate was filtered and dried under vacuum.

Synthesis of the guanidine: to a stirred and ice-cooled solution of amino-thiourea \(H^7\) (161 mg, 0.25 mmol) in ethyl acetate (2 mL), was added triethylamine (70 μL, 0.50 mmol). To the reaction mixture iodine (70 mg, 0.27 mmol) was added in 5 portions over a period of 30 minutes. The reaction was monitored by TLC and after 1 hour was stopped. The product was purified by flash chromatography (silica gel, 50% EE/PE) giving the guanidine \(H^{12}\) as yellow solid (95%).

CCDC 855347 and 855348 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Synthesis of the new compounds

\[(4S,5S)-4,5\text{-Bis-}[\text{isocyanato-diphenylmethyl}]\text{-2,2-dimethyl-1,3-dioxolane} \ (3b):\] to a stirred solution of TADDAMINE 2 (464 mg, 1 mmol) in dichloromethane (10 mL), was added triethylamine (1.2 mL, 9 mmol), and dropwise a solution of triphosgene (297 mg, 3 mmol) in dichloromethane (2 mL). After one hour water was added and the reaction mixture was extracted with diethyl ether (3×10 mL). The reunited organic layers were dried over sodium sulphate and the solvent evaporated. After purification by column chromatography (silicagel – 10%
EE/PE) gave the bis-isocyanate 3b (502 mg, 97%) as a colourless solid. \( \text{Mp} 145 - 146^\circ \text{C}; R_f = 0.45 \) (20% EE/PE); \( [\alpha]_D^{25} = +28.4 \) (c 1.00, CHCl\(_3\)); \( ^1H \text{ NMR (300 MHz, CDCl}_3\) \( \delta \) 7.35-7.15 (m, 20H, \( H_{\text{arom}} \)), 7.28-7.08 (m, 12H, H\_arom), 6.60 (d, J = 7.2 Hz, H\_arom), 6.58 (d, J = 7.2 Hz, H\_arom), 6.50 (s, 2H, \( H_\text{am} \)), 5.54 (s, 2H, CH), 4.78 (dd, J = 14.8 Hz, J = 6 Hz, 2H, \( H_\text{Pr} \)), 4.38 (dd, J = 14.8 Hz, J = 3.2 Hz, 2H, \( H_\text{Pr} \)). HRMS calculated for \( C_{33}H_{28}N_2O_4 \) [M+H]+ 517.2122, found 517.2119.

\( \text{mp} = 88 - 89^\circ \text{C}; \) \( [\alpha]_D^{25} = +28.4 \) (c 1.00, CHCl\(_3\)); \( ^1H \text{ NMR (300 MHz, CDCl}_3\) \( \delta \) 7.35-7.15 (m, 20H, \( H_{\text{arom}} \)), 7.28-7.08 (m, 12H, H\_arom), 6.60 (d, J = 7.2 Hz, H\_arom), 6.58 (d, J = 7.2 Hz, H\_arom), 6.50 (s, 2H, \( H_\text{am} \)), 5.54 (s, 2H, CH), 4.78 (dd, J = 14.8 Hz, J = 6 Hz, 2H, \( H_\text{Pr} \)), 4.38 (dd, J = 14.8 Hz, J = 3.2 Hz, 2H, \( H_\text{Pr} \)). HRMS calculated for \( C_{33}H_{28}N_2O_4 \) [M+H]+ 517.2122, found 517.2119.

1,1’-((4S,5S)-2,2-dimethyl-1,3-dioxolan-4-5-diyl) bis(diphenylmethylenebis(3-methylthiourea) (H1): following the general procedure GP-1 with the mention that instead of the pure amine, a 33% (w/w) methyl amine solution in ethanol (150 \( \mu \text{L}, 1.2 \text{ mmol}) is used, the bis-thiourea \( \text{H1} \) (286 mg, 94%) was obtained as a colourless solid. \( \text{Mp} 200 - 201^\circ \text{C}; R_f = 0.42 \) (1% MeOH/CH\(_2\)Cl\(_2\)); \( [\alpha]_D^{25} = -162.3 \) (c 1.00; CHCl\(_3\)); \( ^1H \text{ NMR (400 MHz, CDCl}_3\) \( \delta \) 7.34 (d, J = 8Hz, 4H, H\_arom), 7.22 (t, J = 8Hz, 4H, H\_arom), 7.14-7.04 (m, 12H, H\_arom), 6.64 (cv, J = 4Hz, 2H, \( H_\text{am} \)), 6.50 (s, 2H, NH), 5.62 (s, 2H, CH), 2.96 (d, J = 4Hz, 6H, \( H_\text{Pr} \)), 1.54 (s, 6H, CH\_Pr); \( ^13C \text{ NMR (101 MHz, CDCl}_3\) \( \delta \) 181.92 (C=S), 141.22, 140.61, 141.22, 140.61, 131.16, 128.82, 127.45, 127.22, 126.66, 123.28, 121.08, 82.63, 66.52, 32.45, 26.49. HRMS calculated for \( C_{35}H_{38}N_4O_2S_2 \) [M+H]+, 611.2509, found 611.2510.

1,1’-((4S,5S)-2,2-dimethyl-1,3-dioxolan-4-5-diy) bis(diphenylmethylenebis- (3-isopropylthiourea) (H2): following the general procedure GP-1 the thiourea \( \text{H2} \) (327 mg, 98%) was obtained as a colourless solid. \( \text{Mp} = 88 - 89^\circ \text{C}; R_f = 0.31 \) (60% EE/PE); \( [\alpha]_D^{25} = +241.6 \) (c 1.00, CHCl\(_3\)); \( ^1H \text{ NMR (300 MHz, CDCl}_3\) \( \delta \) 7.28-6.98 (m, 20H, \( H_{\text{arom}} \)), 6.32 (s, 2H, NH), 6.29 (s, 1H, NH), 6.27 (s, 1H, NH), 5.45 (s, 2H, CH), 4.24 (m, 2H, \( H_\text{PrPr} \)), 1.57 (s, 6H, CH\_Pr), 1.04 (d, 6H, J = 6Hz, CH\_Pr), 0.57 (d, 6H, J = 6Hz, CH\_Pr); \( ^13C \text{ NMR (75 MHz, CDCl}_3\) \( \delta \) 179.35 (C=S), 141.34, 140.64, 130.15, 128.74, 127.43, 127.20, 127.06, 126.63, 107.41, 82.58, 66.58, 48.10 (CH\_Pr), 27.06, 22.36 (CH\_Pr), 21.84 (CH\_Pr). HRMS calculated for \( C_{39}H_{46}N_4O_2S_2 \) [M+H]+ 635.3592 found 635.3593.

1,1’-((4S,5S)-5-(aminodiphenylmethyl)-2,2-dimethyl-1,3-dioxolan-4-5-diy)-diphenylmethyl)-3-methylthiourea (H5): the general procedure GP-2, after 3 days of reflux, gave the amino-thiourea \( \text{H5} \) (239 mg, 89%) as a colourless solid. \( \text{Mp} 292 - 293^\circ \text{C}; \)
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GP-2 gave the amino-thiourea H7: the general procedure GP-2 gave the amino-thiourea H6 (294 mg, 98%) as a colourless solid. Mp 204 - 205°C; Rf = 0.55 (1% MeOH/CH2Cl2); [a]D^25 = -78.6 (c 1.02, CHCl3); ^1H NMR (300 MHz, CDCl3) δ 12.30 (s, 1H, NH), 7.83 (dd, J = 8 Hz, 2H, Harom), 6.59 (s, 1H, NH), 4.50 (d, J = 8 Hz, 2H, H arom), 7.63 (d, J = 8 Hz, 2H, H arom), 7.57 - 7.48 (m, 5H, H arom), 7.44 - 7.35 (m, 6H, H arom), 7.24 - 7.17 (m, 3H, H arom), 7.14 (d, J = 8 Hz, 2H, H arom), 7.09 (d, J = 8 Hz, 2H, H arom), 6.78 (d, J = 8 Hz, 2H, H arom), 6.59 (s, 1H, NH), 4.50 (d, J = 8 Hz, 1H, CH), 3.88 (d, J = 8 Hz, 1H, CH), 2.39 (s, 2H, NH2), 1.27 (s, 3H, CH3), 0.60 (s, 3H, CH3); ^13C NMR (101 MHz, CDCl3) δ 180.46 (C=S), 149.99, 144.46, 144.01, 141.29, 135.87, 130.04, 129.72, 129.52, 128.90, 128.70, 128.50, 128.29, 127.98, 127.77, 127.12, 127.05, 124.08, 122.72, 108.59, 84.99, 80.51, 68.39, 62.65, 27.44, 26.54; HRMS calculated for C_{38}H_{36}N_{3}O_{2}S^{+}[M+H]^+ 645.2530 found 645.2532.

1-(((4S,5S)-5-(aminodiphenylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)diphenylmethyl)-3-(4-chlorophenyl)thiourea (H8): the general procedure GP-2 gave the amino-thiourea H8 (301 mg, 95%) as a colourless solid. Mp 204 - 205°C; Rf = 0.59 (CH2Cl2); [a]D^25 = -77.4 (c 0.99, CHCl3); ^1H NMR (400 MHz, CDCl3) δ 12.40 (s, 1H, NH), 7.81 (d, J = 8 Hz, 2H, H arom), 7.63 (d, J = 8 Hz, 2H, H arom), 7.57 - 7.48 (m, 5H, H arom), 7.44 - 7.35 (m, 6H, H arom), 7.24 - 7.17 (m, 3H, H arom), 7.14 (d, J = 8 Hz, 2H, H arom), 7.09 (d, J = 8 Hz, 2H, H arom), 6.78 (d, J = 8 Hz, 2H, H arom), 6.59 (s, 1H, NH), 4.50 (d, J = 8 Hz, 1H, CH), 3.88 (d, J = 8 Hz, 1H, CH), 2.39 (s, 2H, NH2), 1.27 (s, 3H, CH3), 0.60 (s, 3H, CH3); ^13C NMR (101 MHz, CDCl3) δ 180.43 (C=S), 150.21, 141.45, 141.42, 137.09, 135.88, 131.08, 130.14, 129.72, 129.51, 128.73, 128.70, 128.55, 128.47, 128.44, 128.22, 127.88, 127.72, 127.15, 126.96, 126.23, 108.52, 85.12, 80.55, 68.03, 62.68, 27.48, 26.59; HRMS calculated for C_{38}H_{36}N_{3}O_{2}SCl^{+}[M+H]^+ 634.2285 found 634.2285.

1-(((4S,5S)-5-(aminodiphenylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)diphenylmethyl)-3-(3,5-bis(trifluoromethyl)phenyl)thiourea (H9): the general procedure GP-2 gave the amino-thiourea H9 (313 mg, 84%) as a colourless solid. Mp 186 - 187°C; Rf = 0.62...
(50% EE/EP); \([\delta_1]^{25S} = -92.7\) (c 1.01, CHCl)

\(^1H\) NMR (400 MHz, CDCl) \(\delta\) 12.69 (s, 1H, NH), 7.80 (d, J = 8 Hz, 2H, \(H_{arom}\)), 7.64 (d, J = 8 Hz, 2H, \(H_{arom}\)), 7.57-7.38 (m, 12H, \(H_{arom}\)), 7.34 (s, 2H, \(H_{arom}\)), 7.25 – 7.20 (m, 3H, \(H_{arom}\)), 7.14 (d, J = 4 Hz, 2H, \(H_{arom}\)), 6.78 (s, 1H, NH), 4.48 (d, J = 8 Hz, 1H, CH), 3.89 (d, J = 8 Hz, 1H, CH), 2.40 (s, 2H, NH), 1.30 (s, 2H, CH), 0.64 (s, 2H, CH); \(^13C\) NMR (101 MHz, CDCl) \(\delta\) 180.24 (C=S), 156.03 (C=O), 150.55, 141.10, 141.27, 139.96, 135.85, 131.54, 131.22, 130.77, 129.79, 129.53, 129.03, 128.93, 128.75, 128.53, 128.36, 128.00, 127.79, 127.17, 127.07, 127.04, 118.60, 108.58, 85.05, 80.52, 68.30, 62.70, 27.47, 26.60; HRMS calculated for C\(_{38}\)H\(_{37}\)N\(_3\)O\(_3\) \([M+\text{H}]^+\), 584.2908, found 584.2909.

\(N\)-(3aR)-2,2-dimethyl-4,4,8,8-tetraphenyldihydro-3aH-[1,3]dioxolo[4,5-e][1,3]diazepin-6(7H,8H,8aH)-ylidene)-4-nitroaniline (H12): to a stirred and ice-cooled solution of amino-thiourea H12 (161 mg, 0.25 mmol) in ethyl acetate (2 mL), was added triethylamine (70 \(\mu\)L, 0.50 mmol). To this was added iodine (70 mg, 0.27 mmol) in 5 portions over a period of 30 minutes. The reaction was monitored by TLC and after 1 hour was stopped. The product was purified by flash chromatography (silica gel, 50% EE/PE) giving the guanidine 37c as yellow solid (145 mg, 95%). Mp 164 - 165 °C; \(R_f\) = 0.36 (1% MeOH/CH\(_2\)Cl\(_2\)); \([\delta_1]^{25S} = -239.4\) (c 1.10, CHCl); \(^1H\) NMR (400 MHz, CDCl) \(\delta\) 8.14 (d, J = 9.2 Hz, 2H, \(H_{arom}\)), 7.68 (d, J = 6.8 Hz, 4H, \(H_{arom}\)), 7.45-7.39 (m, 6H, \(H_{arom}\)), 7.29-7.25 (m, 6H, \(H_{arom}\)), 7.19-7.16 (m, 4H, \(H_{arom}\)), 6.96 (d, J = 4.1 Hz, 2H, \(H_{arom}\)), 5.19 (s, 2H, NH), 4.75 (s, 2H, CH), 1.24 (s, 6H, CH\(_3\)); \(^13C\) NMR (75 MHz, CDCl) \(\delta\) 152.70 (CN), 144.73, 142.71, 141.15, 129.09, 128.79, 128.25, 127.90, 127.86, 127.47, 125.72, 123.47, 110.80, 79.88, 66.79, 26.91; HRMS calculated for C\(_{38}\)H\(_{37}\)N\(_3\)O\(_3\) \([M+\text{H}]^+\), 611.2653 found 611.2653.

\(N\)-(3aR)-2,2-dimethyl-4,4,8,8-tetraphenyldihydro-3aH-[1,3]dioxolo[4,5-e][1,3]diazepin-6(7H,8H,8aH)-ylidene)-4-nitroaniline chlorhydrate (H13): to a solution of the guanidine H13 (0.05 mmol) in diethyl ether (0.9 mL) was added a 2M solution of hydrochloric acid in diethyl ether (0.1 mL, 0.2 mmol). A white precipitate was formed instantly. After filtration and drying under vacuum was obtained the guanidine hydrochloride 39c (32 mg, 100%) as a colourless solid. Mp 199 - 200°C; \(R_f\) = 0.68 (5% MeOH/CHCl); \([\delta_1]^{25S} = -201.4\) (c 1.05, CHCl); \(^1H\) NMR (400 MHz, CDCl) \(\delta\) 13.47 (s, H, NH), 8.20 (d, J = 8.8 Hz, 2H, \(H_{arom}\)), 7.47-7.40 (m, 12H, \(H_{arom}\)),
7.37–7.33 (m, 6H, H$_{\text{arom}}$), 7.32–7.25 (m, 5H, H$_{\text{arom}}$), 4.84 (s, 2H, CH), 1.62 (s, 2H, NH), 1.09 (s, 6H, CH$_3$); $^1$H NMR (101 MHz, CDCl$_3$) δ 155.25 (C$_{ipso}$), 146.07 (C$_{ipso}$), 142.16 (C$_{ipso}$), 140.48 (C$_{ipso}$), 138.43 (C$_{ipso}$), 129.36 (C$_{arom}$) – overlap of 2 signals, 129.05 (C$_{arom}$), 128.85 (C$_{arom}$), 128.46 (C$_{arom}$), 127.82 (C$_{arom}$), 125.96 (C$_{arom}$), 124.38 (C$_{arom}$), 112.30 (C$_2$), 69.65 (C$_{Bu}$), 26.78 (CH$_3$).